University of Alberta

MODELING BODY COMPOSITION WITH SPECIAL ATTENTION TO VISCERAL ADIPOSITY

by

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ABSTRACT

In this project we are concerned with understanding the dynamics of body composition for different ethnic and gender groups. The four ethnic groups specific to our study are: Aboriginal, Chinese, European, and South Asian.

We describe the dynamics of body composition using an existing system of ordinary differential equations to describe fat and lean mass change. We expand this model by including a previously determined equation to account for VAT. We parameterize the model using a database of body composition data segregated by gender and ethnicity.

We determine that body composition change is affected by gender and ethnicity. These results are important because they might help to describe why some ethnic/gender groups develop certain obesity related diseases while others do not. Also, the results could be used to direct individuals to a diet that does not promote the accumulation of VAT.

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Chapter 1

Introduction

In this thesis, we discuss factors that influence body weight change in humans. Specifically, we discuss how body weight is influenced by gender and ethnicity for various changes in diet. Studies such as these are important since increasing rates of obesity have been reported among many ethnic groups [20]. In particular, in Canada, obesity is becoming a great problem for individuals of Aboriginal and South Asian populations [1]. Studies show that, today, the rates of obesity in Aboriginal populations in North America are almost double the rates in Europeans [21]. Interestingly, in the Aboriginal populations, the prevalence of cardiovascular disease has also been increasing, whereas it has been decreasing for other populations in Canada [2]. Reasons for this may be directly linked to the increasing rates of obesity within this population. In many cases, it has been found that many disease risks, such as insulin resistance and cardiovascular disease, are linked to obesity [24]. It has also been shown that some ethnic groups, as well as gender groups, are more prone to develop these diseases than others.

Alarmingly, obesity is becoming a worldwide epidemic, and studies that compare weight change within various ethnic (as well as gender) groups are few [20]. Because obesity has been found to be linked to various disease risks, it is important that these types of studies are completed. Here, we will take a mathematical approach to understanding the mechanism of weight change

between various ethnic/gender groups. Specifically, we will use ordinary differential equations as a tool to describe weight change. We will attempt to interpret our results in a biological sense, in hopes that they can be used clinically to help individuals attain a healthy body weight.

In Section 1.1 of this chapter, we discuss the meaning of body composition. Here, we also describe the factors that influence changes in body composition, as well as methods that can be used for measuring body composition. In Section 1.2, we discuss the health risks involved with certain types of obesity. Specifically, we describe the health risks that are involved with having too much fat around the abdominal region of the body. In the final section of this chapter, Section 1.3, we give an overview of the thesis.

1.1 Body Composition

The makeup of fat and lean tissue in the body is called body composition [35], where the sum of fat and lean tissue equals total body weight. Lean tissue corresponds to the proteins and carbohydrates that make up the muscle, bone, and organs of the body. It also corresponds to the water associated with proteins and carbohydrates, where about 50 to 60 % of lean tissue corresponds to water. Fat tissue (also called adipose tissue) is found in the marrow of bones, heart, lungs, liver, kidneys, spleen, intestines, muscles, and lipid-rich tissues of the central nervous system. Two specific types of fat tissue are visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT). VAT corresponds to the fat tissue that envelops the vital organs in the abdominal region of the body, and the SAT is the fat tissue that lies under the skin (the fat that we can grab when we pinch ourselves). Having some fat tissue is important and is essential for normal physiological function. However, an excess of fat can be dangerous and contribute to many different health risks [35].

It has been shown that fat accumulation in some areas of the body is more dangerous than others. Specifically, it has been shown that fat accumulation in the abdominal region of the body imparts significant risk to diseases such

as cardiovascular disease and diabetes [21]. Visceral adipose tissue has been proven to be a greater risk factor for such diseases than subcutaneous adipose tissue. However, truncal subcutaneous adipose tissue may also be a health risk, since it has been associated with insulin resistance in minority groups [3]. We will discuss, in better detail, the health risks involved with abdominal obesity in Section 1.2.

1.1.1 What Affects Body Composition?

Understanding the mechanisms governing body composition is a vital component in helping individuals obtain and maintain a healthy weight. In other words, it is important to understand the factors that control body weight gain and loss, so that we can better educate people on how to live a healthy lifestyle.

Certain factors affecting body composition are easier to understand than others. One such factor is diet, that is, the amount and type of food we take in each day. Another factor affecting body composition is energy expenditure, in the form of physical activity. It has been shown that individuals who engage in an active life style tend to be leaner and have a smaller body weight than those who are less active [35]. These two factors are considered by many to be the primary factors that help to regulate body weight. If an individuals food consumption is balanced by the amount of energy they expend, then an individual will stay at a constant body weight. However, in general, we do not fully understand how an individuals body matches their total intake of food with the amount of energy they expend over long periods of time.

There are many other factors that affect body composition that are not well understood. Two such factors are ethnicity and gender. There are few studies discussing this topic and, as a result, the mechanisms describing how such factors affect body composition are not well known. In this thesis, we are interested in reaching a better understanding of how these two factors influence body composition change.

1.1.2 Quantifying Body Composition

Body composition can be measured using a number of different methods. Anthropometric type measurements are the easiest and most cost efficient way of measuring body composition. These measurements include waist circumference (WC), hip circumference (HC), body mass index (BMI), and skinfolds [35].

Waist circumference is used as a measure of central adiposity and is determined by locating the upper hip bone and placing a measuring tape around the abdomen (ensuring that the tape measure is horizontal). The tape measure should be snug on the body but should not compress the skin.

Hip circumference is measured around the widest part of the hip area and is measured in the same way as waist circumference. This measurement, by itself, does not have clinical importance, and is generally used to determine the waist to hip ratio (WHR). That is, the hip circumference divided by the waist circumference. This measurement looks at the proportion of fat stored around the waist and in the hip/buttocks area. In many cases, individuals having extra weight on their waist are at a higher risk to develop diseases such as heart disease and diabetes than those carrying weight around their hips and thighs. In this way, WHR can be a good indicator of overall health [25].

BMI is also used as an indicator of overall health. However, it is thought to be less efficient at predicting health risks than WC and WHR measurements [21]. BMI is measured by dividing an individual's total weight by the square of his/her height.

Skinfolds are measured using calipers. The calipers are used to pinch the skin in a given area of the body. The amount of skin and fat that is grabbed by the calipers is measured and compared to a standard value. This type of measurement is used to measure subcutaneous adipose tissue.

There are other types of body composition measurements that are more accurate. However, increased accuracy is generally accompanied by increased cost and time. Two such methods are computed tomography scans (CT scans)

and dual energy x-ray absorptiometry scans (DEXA scans) [35]. CT imaging uses special x-ray equipment to produce multiple images (or pictures) of the inside of the body and a computer to join them together in cross-sectional views of the area being studied. This type of calculation is useful for determining visceral adipose tissue mass. DEXA scans are used to measure bone mineral content, bone mineral density, fat-free mass, and to provide estimates of percent body fat.

1.2 Visceral Adiposity and Health Risks

As stated previously, understanding the dynamics of body composition is important for many reasons, the most important reason being related to good health. It is known that overfeeding and lack of physical activity lead to weight gain, and in certain circumstances this type of ill treatment of the body can lead to obesity [35]. It is also known that extreme underfeeding can lead to excessive weight loss, and in some cases can lead to diseases such as anorexia [35]. By understanding how changes in body composition differ between people of certain gender and ethnicity, we can get a better idea of how to help those suffering from extreme weight gain or weight loss.

Today, obesity is becoming much more problematic. Populations where once obesity was rare show alarming increases in the number of those affected by the disease [21, 22]. Recent studies have shown that minority groups (such as Hispanics and African Americans) living in the United States have higher rates of overweight and obesity as compared to caucasians [3]. A survey of 63 nations, published in the American Heart Association's medical journal, showed that Canadian adults, both male and female, are the most obese. Although this survey doesn't represent the overall Canadian adult population, many people are very concerned with these results [32].

It has been found that high amounts of VAT impart significant risks to the complications of obesity (less so than subcutaneous fat). Risks include insulin resistance, diabetes mellitus, cardiovascular disease and atherosclero-

sis [21, 22]. Also, it has been shown that abdominal adiposity, specifically visceral adiposity, is more strongly associated with risk factors for cardiovascular disease than any other adipose tissue region [21]. Cardiovascular disease, along with the risks listed above, are associated with a disease called the metabolic syndrome [24]. The main features of the metabolic syndrome include insulin resistance, hypertension (high blood pressure), cholesterol abnormalities, and an increased risk of blood clotting. In almost all cases, patients suffering from this syndrome are overweight or obese, most often in the abdominal region of the body.

Studies have shown that ethnic-specific differences exist in VAT mass accumulation [21]. For example, one such study has recorded differences in VAT between African Americans and Europeans [21]. African American men have smaller amounts of VAT, whereas African American women have similar or smaller amounts of VAT than Europeans for a given body fat mass. Recently, Lear *et al.* have completed a study to compare VAT in Aboriginal, Chinese, and South Asian populations with VAT in European populations [21, 22]. Studies concluded that Chinese and South Asian populations had a relatively greater amount of VAT while no significant differences were noticed between the Aboriginal and European populations.

1.3 Goals and Outline

In this thesis, we will explore the effect of diet, energy expenditure, gender, and ethnicity on the dynamics of body composition. To do this, we consider a two compartment body composition model. Specifically, we assume that body weight can be separated into two distinct compartments: lean mass and total fat mass. We also consider a sub compartment of total fat mass, that is, VAT mass. Figure 1.1 is a schematic of the model we wish to study, where the shaded boxes correspond to the compartments specific to our model. Our goal is to attain a better understanding of how gender and ethnicity play a role in body composition change. Specifically, we wish to address the question

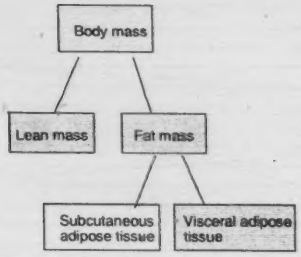


Figure 1.1: Schematic of the Model

of whether certain gender/ethnic groups accumulate a greater amount of VAT than others. The answer to this question becomes important when trying to clinically diagnose individuals who are at risk for diseases such as the metabolic syndrome. Also, because anthropometric methods for calculating obesity are cheaper than other methods (such as CT scanning), it may be of importance to define proper cut-off parameters based on ethnicity and gender. In the final chapter, Chapter 6, we will discuss how such cut-off parameters may be established.

This thesis in composed of six chapters. In Chapter 2, we give a review of previous modeling efforts used to describe body weight change. Here, we consider a pair of differential equations, developed by Hall *et al.* [14], that describe individual change of lean mass and total fat mass as a function of time. Important factors that influence these changes include diet and total energy expenditure. In Chapter 3, we discuss a recent clinical study that examines the medical risks involved with abdominal obesity. In this study, an extensive data set was developed by Lear *et al.* [20], comprising of body composition measurements for individuals of different genders and various ethnic backgrounds. In Chapter 4, we extend the modeling efforts of Chapter 2 to account for gender and ethnicity. This extension is aided by use of the data set developed by Lear *et al.* [20] and described in Chapter 3. Also, in this chapter, we discuss the development of an allometric equation that accurately describes the relationship between VAT and total fat mass [15]. Therefore,

by calculating the total fat mass of an individual as a function of time, we will be able to describe their VAT mass as a function of time. In this chapter, we also complete a full mathematical analysis of our extended model. In Chapter 5, we present and discuss the results found from implementation of our model, described in Chapter 4. We will complete various overfeeding and underfeeding simulations for eight distinct populations: Aboriginal, Chinese, European, and South Asian men and women. Here, we will look at changes in total fat mass, lean mass, and VAT mass over an extended period of time. In this chapter, we will also complete a sensitivity analysis to mathematically explain the results of the overfeeding and underfeeding simulations. In our final chapter, Chapter 6, we give a summary of our research, state the major conclusions, and discuss future research avenues.

Chapter 2

Review of Previous Modeling Efforts

It is known that changes in fat and lean mass, when induced by nutrition, usually occur simultaneously. However, it is difficult to quantify exactly how these changes occur and the extent to which they occur [11]. In recent years, there have been numerous studies completed to better understand how such processes work. In Section 2.1, we discuss a relationship between lean mass (L) and total fat mass (F), where the sum of fat and lean mass is the total body weight (W), derived by Forbes [10]. In Section 2.2, we discuss an extension of Forbes' work, by Hall [13], that describes the contribution of lean mass to a macroscopic change in body weight. Finally, in Section 2.3, we discuss an existing model, developed by Hall et al [14], that describes how fat and lean mass change over extended periods of time, as well as the factors that influence this change. This model will be the basis for the future modeling efforts of Chapter 4.

2.1 The Forbes Equation

Forbes' interest in quantifying body composition (F and L) began after making observations on individuals who were extremely overweight or malnourished.

He noticed that obese individuals generally have a large amount of lean mass as well as an excess of fat in comparison to individuals who are at a normal, healthy weight. As well, for obese individuals, he noticed that lean mass tends to increase with increasing degrees of obesity. Also, he found that underweight individuals, due to malnutrition, have both reduced lean and fat mass. These observations made it apparent to Forbes that there is a relationship between fat and lean mass. He was thus motivated to construct a study to describe this relationship [10].

Forbes' study consisted of 164 women of similar stature (i.e., women of height 1.56 - 1.7m tall), where the women were grouped according to weight. These groups included women suffering with anorexia nervosa, women of healthy weight (as determined by BMI measurements), and women with varying degrees of obesity. After grouping these women and measuring their body fat and lean mass content, Forbes found that lean mass and total fat mass are related by the following empirical expression,

$$L = 10.4 \ln F + 14.2, \tag{2.1}$$

with F and L in Kg, shown in Figure 2.1. Forbes theorized that long-term changes in body composition could be described by movement along this curve. Basically, Forbes suggested that one should be able to make predictions about the compositions of weight gains and losses in individuals using this curve. It is apparent that for very small F, specifically 0 Kg $< F <$ 0.26 Kg, L will be negative. This is not a problem since this situation is not realistic (it is impossible for an individual to have such small contributions of F), so it will not be considered.

From equation (2.1), we see that a change in the parameter 14.2 either shifts the Forbes curve up or down, where higher values of this parameter corresponds to leaner individuals. It would be fair to hypothesize that this parameter would be higher for men than for women, as males are generally more lean than females.

By differentiating equation (2.1) with respect to F, a relation between change in lean mass and change in fat mass is determined,

$$\frac{dL}{dF} = \frac{10.4}{F}. \tag{2.2}$$

This equation, derived for infinitesimal weight change, represents the slope of the curve in Figure 2.1, the Forbes curve. Here we note that the slope is a hyperbolic function of F and is steep at low values of F and flatter at higher values of F. Biologically, this means that during periods of weight gain, smaller individuals are likely to gain more lean mass than fat mass, whereas heavier individuals are likely to gain more fat mass than lean mass.

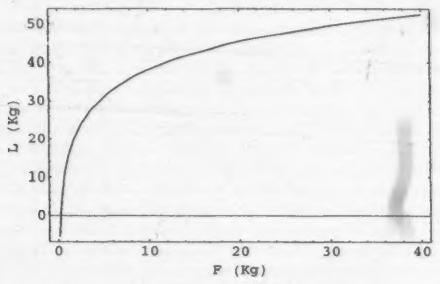


Figure 2.1: Forbes curve, from equation (2.1)

Using equations (2.1) and (2.2), Forbes was able to make a number of predictions about weight gain and loss. He was able to validate these predictions by obtaining published data on diet-induced weight changes. His first prediction was that during a fast, obese individuals will lose less lean mass relative to body fat than thin people. This prediction comes from the fact that the right hand side of equation (2.2) is smaller for obese people than for thin people. Also, Forbes predicted that heavier individuals will have a smaller contribution of lean mass to a total weight loss on low-energy diets. This is seen by setting $dW = dF + dL$, or $dF = dW - dL$, and rewriting equation (2.2) as,

$$\frac{dL}{dW} = \frac{10.4}{10.4 + F}. \tag{2.3}$$

At smaller values of F, the derivative dL/dW is much larger than at higher values of F.

Even though Forbes' theory has proven itself as a useful tool, there are a number of shortcomings. One shortcoming is that Forbes' work has been derived for infinitesimal weight change and may not be useful when dealing with large weight loss or gain. This shortcoming is looked at more closely in the next section. Another shortcoming of Forbes' theory is that it has been derived using data collected from women only. Also, there is no information regarding the ethnic background of the women studied. This raises the question of whether or not the empirical function (2.1) accurately describes the relationship between L and F for both genders and for different ethnicity. This is the question we wish to address in Chapter 4.

2.2 Extension of Forbes' Equation

Forbes equation (2.2) has been derived for infinitesimal weight change and is not valid for large changes in body weight. For example, Forbes theory is not useful for describing massive weight loss in individuals following various bariatric surgery procedures [13]. Noticing this disadvantage, Hall [13] has revisited Forbes' theory and has extended it to account for macroscopic changes in weight. For a macroscopic change of W, ΔW, Hall considers the expression $\Delta W = \Delta F + \Delta L$. He then rewrites this expression as $\Delta L = \Delta W - \Delta F$. Dividing ΔL by ΔW and rewriting, he obtains an expression describing the contribution of L to a macroscopic weight change,

$$\frac{\Delta L}{\Delta W} = 1 - \frac{\Delta F}{\Delta W} = 1 - \frac{F_f - F_i}{\Delta W}, \tag{2.4}$$

where F_f and F_i are the final and initial values of F, respectively, and $\Delta F = F_f - F_i$. Hall's goal was to rewrite this equation so that only ΔW and F_i were in the right-hand side of the equation. If this could be accomplished, it would be a powerful tool in predicting macroscopic body composition change

for a given change in body weight and an initial fat mass. We reproduce the derivation here. To start, we rewrite Forbes equation (2.1), expressing F in terms of L, and obtain the expression

$$F = \exp\left(\frac{L - 14.2}{10.4}\right). \tag{2.5}$$

Without loss of generality, this can be written as

$$F_f = \exp\left(\frac{L_f - 14.2}{10.4}\right). \tag{2.6}$$

Now, rewriting $\Delta W = \Delta F + \Delta L$ as $\Delta W = (F_f - F_i) + (L_f - L_i)$ and rearranging, we arrive at

$$L_f = \Delta W + L_i + F_i - F_f. \tag{2.7}$$

Substituting this expression into equation (2.6) and rewriting L_i using Forbes' equation (2.1), we obtain

$$F_f \exp\left(\frac{F_f}{10.4}\right) = \exp\left(\frac{\Delta W}{10.4}\right) \exp\left(\frac{F_i}{10.4}\right) F_i. \tag{2.8}$$

This is a transcendental equation and can be solved for F_f using the Lambert W Function [5], W_L, to give,

$$F_f = 10.4 W_L\left(\frac{1}{10.4} \exp\left(\frac{\Delta W}{10.4}\right) \exp\left(\frac{F_i}{10.4}\right)\right) F_i. \tag{2.9}$$

The Lambert W function is defined to be the inverse of the function $W \mapsto We^W$. Substituting equation (2.9) into equation (2.4), we finally arrive at the expression Hall aimed for,

$$\frac{\Delta L}{\Delta W} = 1 - \left(\frac{10.4 W_L}{\Delta W}\left[\frac{1}{10.4} \exp\left(\frac{\Delta W}{10.4}\right) \exp\left(\frac{F_i}{10.4} F_i\right)\right]\right) + \frac{F_i}{\Delta W}. \tag{2.10}$$

This equation depends on the sign and magnitude of body weight change, ΔW, as well as the initial fat mass, F_i. In the limit as ΔW goes to zero, the

equation reduces to equation (2.3).

Hall found that data from over-feeding and under-feeding experiments fit well to equation (2.10) [13]. For modest weight change, he also found that Forbes' equation (2.3) compared favorably. However, for large weight change, such as weight loss following bariatric surgery, he found that equation (2.3) underestimated lean mass loss, whereas the new equation (2.10) better estimated the change in lean mass.

2.3 Basic Model of Body Composition and Substrate Utilization

Recently, Hall *et al.* [14] have completed a study that clearly defines a mathematical relationship between long-term changes of body composition and the substrate utilization (fat and nonfat oxidation) required to produce these changes. The purpose of this study was to determine how substrate utilization quantitatively adapts to a given energy imbalance in order to produce the long-term body composition changes proposed by Forbes [10].

Hall *et al.* first derived a simple expression to describe how interactions between diet, energy expenditure, and substrate utilization are quantitatively connected to changes in body composition. Energy expenditure, food intake, and initial body composition are measured experimentally and used as model inputs. The model is then used to predict changes in substrate utilization and body composition.

Since the model will be used as a basis for the research in this thesis, we describe it in detail below. In Section 2.3.1, we will discuss how energy is used to maintain the body. In Section 2.3.2, we will give a detailed description of the model, and finally, in Section 2.3.3, we will describe the model parameters.

2.3.1 Background: Energy Utilization of the Body

Before going any further, it is important to understand the basic processes underlying the dynamics of body composition. These processes are all governed by the law of energy balance (also known as the first law of thermodynamics) [29]. For an individual whose weight does not fluctuate, the bodies energy remains at equilibrium, meaning that the energy they consume (through eating) is equal to the energy that they expend (through processes such as physical activity and metabolism of food). This fact is what governs the dynamics of body composition. When we eat food we take in chemical energy. Our body then converts this chemical energy, through various metabolic processes, to other forms of energy for the body's work [35]. The sum of all chemical processes in a living organism by which energy is made available for the functioning of the organism is called metabolism [35]. In our body, there are four basic forms of energy required for normal function: chemical, electrical, mechanical and thermal. Chemical energy is converted to electrical energy in brain and nerve activity, it is converted to mechanical energy in muscle contraction, and it is converted to thermal energy to regulate the body's temperature. If energy input is greater than what is required for bodily function, energy may be stored in the form of fat or lean tissue to account for this imbalance, causing an increase in weight [35].

2.3.2 The Model

Using the laws of energy balance, described in the previous section, Hall *et al.* first consider the following macronutrient (carbohydrate, protein, and fat) balance equations,

$$\rho_F \frac{dF}{dt} = I_F - FatOx \tag{2.11}$$

$$\rho_L \frac{dL}{dt} = I_L - NonFatOx, \tag{2.12}$$

where F and L correspond to total fat and lean mass, I_f is the metabolizable intake rate of fat, I_L is the sum of the metabolizable intake rates of protein and carbohydrate, $FatOx$ is the oxidation rate of fat, $NonFatOx$ is the oxidation rate of lean mass, and ρ_F and ρ_L are the energy densities of F and L change respectively. It is clear from the model that a change in body composition is proportional to the amount of energy we take in (through food) minus the energy we expend (through the metabolic processes of fat and nonfat oxidation).

Expressions for $FatOx$ and $NonFatOx$ can be found in terms of F, L, I_F, I_L, and the total energy expenditure E. To determine such expressions, we let f_F be the fraction of the energy expenditure accounted for by fat oxidation, and $1 - f_F$ be the fraction of energy expenditure accounted for by nonfat oxidation (where f_F is a dimensionless parameter and $0 \leq f_F \leq 1$. Now we can rewrite equations (2.11) and (2.12) as,

$$\rho_F \frac{dF}{dt} = I_F - f_F E \tag{2.13}$$

$$\rho_L \frac{dL}{dt} = I_L - (1 - f_F)E, \tag{2.14}$$

where $E = FatOx + NonFatOx$. If we divide equation (2.14) by equation (2.13), we obtain the expression

$$\frac{\rho_L}{\rho_F}\frac{dL}{dF} = \frac{I_L - (1 - f_F)E}{I_F - f_F E}. \tag{2.15}$$

Now, substituting the differential form of Forbes equation, (2.2), into (2.15), we arrive at an expression for the fat oxidation rate ($f_F E$),

$$f_F E = \frac{(\frac{C}{F})I_F - I_L + E}{1 + (\frac{C}{F})}, \tag{2.16}$$

where $C = 10.4\frac{\rho_L}{\rho_F}$. It is important to note that the fraction C/F is generally positive and less than 1 ($C \approx 2$). As a result, when the nonfat intake rate, I_L, is fixed, wide variations in fat intake, I_F, have little impact on the fat

oxidation rate, $f_F E$. However, when I_F is fixed, alterations in I_L create a significant change in $f_F E$.

The model shows that diet plays a dominant role in determining substrate utilization rates. In particular, it predicts that I_F has much less influence on fat and nonfat oxidation rates as compared to I_L. The model agreed well with data and indirect calorimetry, which showed that addition of excess dietary fat had little impact on macronutrient oxidation rates in comparison with the dietary carbohydrate or protein (data taken from underfeeding and overfeeding in human males) [14]. Even though the model accurately describes how substrate utilization adapts to changes in diet, energy expenditure, and body fat, the physiological mechanisms for these adaptations have not yet been specified.

Hall's model, after substitution of equation (2.16) into equations (2.13) and (2.14), can be written as follows

$$\rho_F \frac{dF}{dt} = I_F - \left(\frac{(\frac{C}{F})I_F - I_L + E}{1 + (\frac{C}{F})} \right), \tag{2.17}$$

$$\rho_L \frac{dL}{dt} = I_L - E + \left(\frac{(\frac{C}{F})I_F - I_L + E}{1 + (\frac{C}{F})} \right). \tag{2.18}$$

Here we give an example of how one can produce solution curves for F and L by numerically integrating equations (2.17) and (2.18). In this model we will use inputs taken from an overfeeding study by Diaz *et al.* [7]. First, we take $I_F = 1956.15$ Kcal/day and $I_L = 2701.35$ Kcal/day. In this study, energy expenditure E was recorded every 7 days for a total time period of 42 days. These data points were extracted from the Diaz paper by Hall *et al.* [13] and then interpolated. Figure 2.2 is a plot of the interpolated energy function. Recall that once I_F, I_L, and E are known, one can calculate the fat and nonfat oxidation rates ($FatOx$ and $NonFatOx$) by substituting these inputs into equation (2.16). Figure 2.3 corresponds to $FatOx$ and $NonFatOx$, as well as the inputs I_F and I_L. Here we see that $NonFatOx$ increases to almost the same rate as I_L, whereas $FatOx$ increases to reach only about 50 % of I_F.

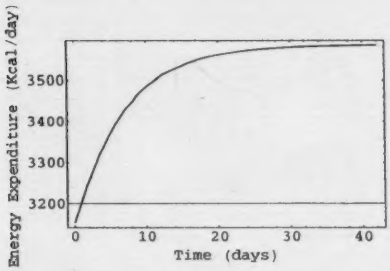


Figure 2.2: Interpolated energy expenditure function.

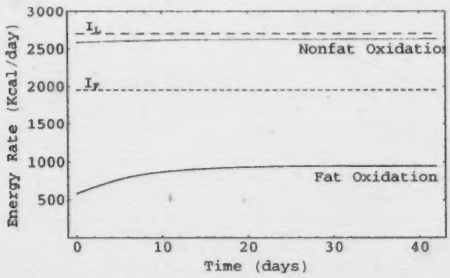


Figure 2.3: Fat and nonfat oxidation rates, as well as fat and nonfat intake rates.

Figure 2.4 shows the solution curves for F, L, and total body weight W as functions of time. Note that the increase in F is larger than the increase in L. This has to do with the fact that $FatOx$ is lower than $NonFatOx$ (as shown in Figure 2.3).

It is important to note that, in this example, we have numerically integrated the interpolated energy expenditure function E in order to determine solution curves for F and L. In Chapter 4, we will describe E in terms of F, L, and total intake rate I_T, so that E will not need to be clinically measured in order to implement this model.

2.3.3 Model Parameters: Definitions and Units

Energy Expenditure (E)

Energy imbalance is a leading cause of many serious health problems [35, 31]. When an individual expends less energy then they consume, they generally

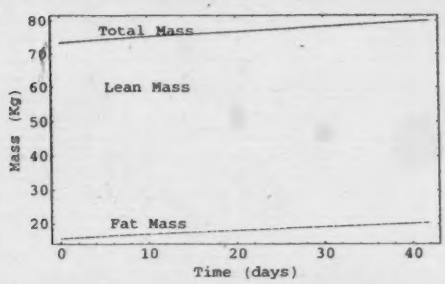


Figure 2.4: Fat mass, lean mass, and total body weight as a function of time.

gain weight and, in extreme cases, they can become obese. Similarly, when an individual expends less energy than is required for normal bodily function, they generally lose weight [35, 31].

Total energy expenditure (E) can be divided into three main components: physical activity (PA), the thermic effect of food (TEF), and the resting metabolic rate (RMR), also called the resting energy expenditure (REE) [31].

Physical activity (PA) is one of the easiest components of total energy expenditure to understand. It is the energy expended both during and after physical activity and accounts for 15 to 30 percent of E. The more one exercises, the more energy one expends.

The second component of total energy expenditure is the thermic effect of food (TEF) and includes the energy required for absorption, metabolism, and storage of food within the body. Absorption and transport require a relatively small amount of energy, while a larger proportion of the energy goes into the synthesis of protein, carbohydrates, and fat, as this is required for the constant renewal of body tissue and for storage. In most cases, about 10 percent of the body's E is accounted for by TEF.

The last and largest component of total energy expenditure is the REE, accounting for 60 to 70 percent of E. It is defined as the sum of all internal chemical activities that maintain the body at rest and is the energy expended while resting in a neutral environment 8-12h after eating or physical activity. It includes the costs of maintaining the integrated systems of the body and

the homothermic temperature at rest [35, 31].

Energy expenditure is measured using a number of different methods. To measure REE, one may use indirect methods, since direct methods, such as direct calorimetry, are outdated [35]. In indirect calorimetry, an instrument (sometimes called a metabolator) is brought close to the individual. As the individual takes breaths through a mouthpiece, the ratio of carbon dioxide (CO_2) to oxygen (O_2) is measured, while the subject is at rest. The metabolic rate is calculated from the rate of oxygen utilization, as more then 95 percent of the energy expenditure is derived from metabolic reactions with oxygen. This method is equivalent to measuring the amount of the heat that escapes from the body and is much more cost efficient than direct methods. Most commonly empirically derived equations such as the Weir equation [34] are used to measure REE. This equation includes O_2 consumption, CO_2 production, as well as nitrogen excretion. TEF is generally measured as a percentage of a person's diet, and PA can be measured using the oxygen consumption method of indirect calorimetry [35, 31].

The International (SI) unit of energy and heat is the Joule (J). The Joule is defined as the work done by the force of 1 Newton acting over a distance of 1 meter. The term calorie refers to a unit of heat measure, where 1 calorie is equal to 4.187 Joules. The calorie used in nutritional sciences is different from the calorie used in other sciences. It is called the large calorie, and is written as the Calorie (Cal). Here, 1 Calorie = 1000 calories (or 1 kilo calorie). 1 Calorie is defined as the amount of heat required to raise the temperature of 1 kilogram (Kg) of water 1 degree Celsius [35].

Fat Oxidation and Nonfat Oxidation ($FatOx$ and $NonFatOx$)

Fat oxidation and nonfat oxidation are the two components that make up substrate utilization, where a substrate is defined as the specific organic substance on which a particular enzyme acts to produce new metabolic products [35]. Substrate utilization describes how the body metabolizes fat and nonfat [35], where to metabolize means to produce a substance through metabolism. Here,

metabolism is the sum of all the various biochemical and physiologic processes by which the body grows and maintains itself and breaks down and reshapes tissue, transforming energy to do its work. Here, the addition of fat oxidation and nonfat oxidation equals the total energy expenditure and the units of both fat oxidation rate and nonfat oxidation rate are Kcal/day.

Intake Rates (I_F and I_L)

Intake rates are measured by counting the amount of Kcal of fat and lean mass one eats in a day. These rates have the units of Kcal/day.

Energy Densities (ρ_F and ρ_L)

As stated above, ρ_F and ρ_L are the energy densities of fat and lean mass change. In this project, we neglect de novo lipogenesis (synthesis from glucose of fatty acids), as it is generally only a minor contributor to weight gain and loss. Here, we take $\rho_F = 9400$ kcal/kg and $\rho_L = 1800$ kcal/kg [14].

Chapter 3

Multicultural Community Health Assessment Trail (M-CHAT)

In the previous chapter, we have described a model that requires input for implementation. Specifically, we require a data set that includes individual measurements of body composition (F and L), energy expenditure (E), and intake rates (I_F and I_L). Later, in Chapter 4, we will discuss extending the previous model to account for gender and ethnicity. Therefore, we will also require data on subject gender and ethnicity. In this chapter, we describe such a data set, obtained by Lear and colleagues of the Lipid Clinic at St. Paul's Hospital in Vancouver, BC [20]. In Section 3.1, we will describe the study design [20]. Here we will discuss in detail the type of data collected, why it was collected, and how it was collected. In Section 3.2, we will discuss the results of the study [21, 22].

3.1 Study Design

It has been suggested that body fat distribution differs between ethnic groups. As body fat distribution may be an important factor when considering risk for

disease, it is possible that some ethnic groups are more prone to developing certain diseases than others. A recent study, called the Multicultural Community Health Assessment Trail (M-CHAT) [20], has been completed by Lear *et al.* to investigate differences in body fat distribution between different ethnic populations. The goal of the study was to compare body fat distribution, specifically visceral adipose tissue distribution, in four distinct ethnic populations, and for both genders [21]. The four ethnic populations used in this study were Aboriginal (Canadian Indigenous peoples), Chinese (individuals from China, Taiwan, and Hong Kong), European (individuals from Continental Europe, the United Kingdom, and Ireland), and South Asian (individuals from Pakistan, India, and surrounding nations). The study consisted of a total of 829 subjects, where there was an approximate equal distribution of male and female populations, corresponding to a total of 8 groups with approximately 100 people per group. Within each gender/ethnic group, there was an approximately equal representation of individuals having a BMI between 18.5 to 24.9 Kg/m^2, 24.9 to 29.9 Kg/m^2, and a BMI greater than 30 Kg/m^2. These BMI ranges correspond to healthy individuals, overweight individuals, and obese individuals, respectively. To be part of this study, a number of inclusion criteria had to be satisfied. Some of the main criteria state that individuals are not to have any major health problems and that an individual's weight should show no significant fluctuations for the three months proceeding the study. These criteria, as well as others, are explained in detail and can be found in the original project proposal [20].

Data such as subject gender, ethnicity, and BMI has been recorded into one extensive data set. Other types of data include lean and fat mass measurements for each individual, as well as information about the fat content of specific body parts (e.g., legs, arms, body trunk, and abdomen). Fat mass measurements were completed using dual energy X-ray absorptiometry scans (DEXA scans), and subject total body mass was determined using a standard beam scale. Lean mass was determined by calculating the difference between total body mass and total fat mass. Also, total abdominal adipose tissue

(TAT) and visceral adipose tissue (VAT) measurements were completed using computed tomography scans (CT-scans). Subcutaneous abdominal adipose tissue (SAT) was calculated as the difference between TAT and VAT.

Besides giving detailed information about mass measurements, the data set also includes information on individual energy expenditure due to physical activity (E, based on recall of activities completed in past year), diet (I_L and I_F, based on a 3 day assessment), and height (H). The particular data that will be used in the modeling efforts of Chapter 4 are summarized in Table 3.1.

After completion of the first study, a second study was initiated by Lear *et al.* to determine an accurate way of measuring health risks such as atherosclerosis and cardiovascular disease [22]. Obesity is an independent risk factor for both atherosclerosis and cardiovascular disease, but not all people who are obese, as measured by BMI, develop such diseases. In recent studies, it has been concluded that waist circumference (WC) measurements and waist-to-hip ratio (WHR) measurements are associated with an increased risk of cardiovascular disease. It is believed that this increased risk, associated with high amounts of abdominal fat, is mostly due to VAT. Lear *et al.* believe that an increased level of VAT, regardless of BMI, may be an indicator of cardiovascular disease, and may put individuals at a higher risk for developing atherosclerosis. Here, Lear *et al.* hypothesize that the association between VAT and atherosclerosis is independent of total body fat, established risk factors (such as smoking and quality of life), and measures of central adiposity (WC and WHR). To complete this study, Lear *et al.* use the same subject information as in the first part of the study, along with information on measurements of carotid artery intima-media (inner area) thickness (IMT) and plaque area [35]. Plaque is described as thickened deposits of fatty material, mostly cholesterol, within arterial walls. If plaque build up is large enough, it may cut off blood supply to the tissue served by the damaged vessel [35]. These measurements were completed using carotid artery ultrasound [17] and the combined value of both IMT area and plaque area is used to measure atherosclerosis.

3.2 Study Results

After completion of the initial study [21], it was found that body fat distribution, as measured by total body fat, TAT, SAT, and VAT, differs among ethnic groups. Most importantly, it was found that the Chinese subjects and most South Asian subjects had more VAT and SAT than Europeans. However, no significant differences in these adipose tissue regions were noticed between the Aboriginal and European groups. Lear *et al.* had originally hypothesized that all non-European groups would have higher amounts of VAT and SAT than the Europeans, especially the Aboriginal group, because the Aboriginal population has both Asiatic roots and elevated rates of obesity and type 2 diabetes mellitus. Lear *et al.* suggest that the unexpected result may indicate that VAT alone does not explain high rates of diabetes.

Interestingly, in the first study, it was also concluded that BMI is an inadequate measure of body fat distribution to specific regions of abdominal adiposity, and that it underestimates VAT in all non-European groups. This conclusion is alarming because BMI is a standard measure, used by many doctors worldwide, of good health [4]. It may be the case that thin people are being told that they are healthy, when in fact they are not (if they have a large amount of VAT). In past studies, such as those by Després [27], it was demonstrated that WC measurements are far better predictors of the risk of heart disease than BMI measurements.

In the second part of Lear *et al.*'s study [22], it is shown that WC and WHR measurements are more indicative of the risk for cardiovascular disease and atherosclerosis than BMI measurements. Results from the second study further show that VAT is the primary region of adiposity associated with atherosclerosis, independent of total adiposity. After adjusting for common risk factors, this relationship remained significant in men, showing that high levels of VAT may have added effects, in addition to WC and WHR, on the development of carotid atherosclerosis. Also, measurements of WC and WHR were found to be highly correlated with VAT. WC and WHR measurements

thus are the preferred clinical measurements for identifying those at risk, as direct measurements of VAT can be expensive.

Measurement	Units	Purpose in Model
Gender	M/F	Used to classify groups
Ethnicity	South Asian/Chinese/ Aboriginal/European	Used to classify groups
Fat Mass	Kg	Used for model fitting and input
Lean Mass	Kg	Used for model fitting and input
BMI	Kg/m^2	Used to classify groups
Height	m	Used to determine BMI
I_F	Kcal/day	Used as input for extended model
I_L	Kcal/day	Used as input for extended model
VAT	Kg	Used as input for extended model

Table 3.1: Data from M-CHAT study to be used in the modeling efforts of Chapter 4.

Chapter 4

Extension of the Previous Modeling Efforts

Forbes' Theory has been used to build the model of substrate utilization and body composition described in Chapter 2. Here, we recall a shortcoming of Forbes' Theory. That is, that the relationship between F and L was derived using data collected from women only, and that the ethnicity of each woman was not taken into consideration. Now, if we question the validity of Forbes equation (2.1), for different genders and ethnicity, we must also question the reliability of the previous model described in Chapter 2.

In Section 4.1, we describe a method of incorporating gender and ethnicity into the existing model. Next, in Section 4.2, we incorporate height into Forbes' relationship between L and F. We do this because Forbes' original theory does not adequately describe the data for all ethnic/gender groups. Also, in Section 4.3, we describe an alternate way of expressing the energy expenditure E. In Section 4.4, we extend our 2-dimensional ODE model to account for changes in visceral adipose tissue. In Section 4.5, we complete a full mathematical analysis of the new model. Finally, in Section 4.6, we produce new Forbes curves for the different ethnic/gender groups. Recall that the original Forbes curve is described by equation (2.1) and is displayed in Figure 2.1.

4.1 Forbes' Parameter A

The first goal in developing our new model is to incorporate gender and ethnicity into the existing model described in Chapter 2. To do this, we start off by assuming a more general form of the Forbes equation (2.1), that is,

$$L = A\ln F + B, \tag{4.1}$$

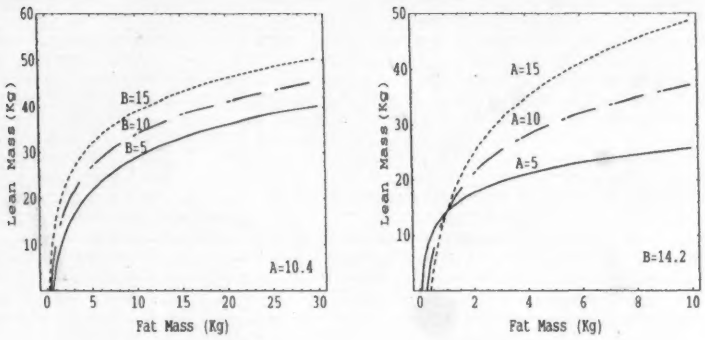
where $A = 10.4$ and $B = 14.2$ in the original Forbes equation (2.1). The parameters A and B will have different values for different ethnic/gender groups, and will be determined by fitting equation (4.1) to data (F and L measurements) from Lear's data set. Here, we denote the parameter A as the Forbes parameter. We recall from Chapter 2 that the parameter B either shifts the Forbes curve (4.1) up or down, where higher values of this parameter correspond to leaner individuals, as shown in Figure 4.1(a).

Taking the derivative of L in equation (4.1) with respect to F, we arrive at the general differential form of Forbes equation,

$$\frac{dL}{dF} = \frac{A}{F}. \tag{4.2}$$

We recall that A/F is the slope of equation (4.1). For a fixed value of A, the curve will be steeper at low values of F and flatter at high values of F. Biologically, this means that during periods of weight gain, smaller individuals are likely to gain more lean mass than fat mass, and heavier individuals are likely to gain more fat mass than lean mass.

If we vary A and consider a fixed weight gain, we can make the observation that an individual with a large value of A and starting at a low percentage of body fat will gain a greater percentage of lean mass than an individual with a smaller value of A and starting at the same percentage of body fat, as shown in Figure 4.1(b). For individuals starting at higher percentages of body fat, gains in lean mass are almost equivalent regardless of the value of A, since the slope of the Forbes curve flattens at high values of F.



(a) (b)

Figure 4.1: Effect of changing parameters A and B in Forbes equation (4.1). (a) Increase in A for fixed B. (b) Increase in B for fixed A.

It is interesting to note that the parameter A also shifts the Forbes curve up or down, as well as the parameter B. Here we note that individuals at a given body weight and having a high value of the parameter A will be leaner than individuals at the same body weight but having a low value of the parameter A.

Our next step is to include the Forbes parameter A into the previous model of fat and lean mass change, described in Chapter 2 by equations (2.17) and (2.18). Here we recall the expression describing the fat oxidation $f_F E$, described in Chapter 2 by equation (2.16). Substituting equation (4.2) into equation (2.15), we arrive at a more generalized form of the fat oxidation,

$$f_F E = \frac{A\frac{\rho_L}{\rho_F}\frac{I_F}{F} - I_L + E}{1 + (A\frac{\rho_L}{\rho_F}\frac{1}{F})}. \tag{4.3}$$

Unlike equation (2.16), our new expression for $f_F E$ depends on the Forbes parameter A, as well as the initial intake rates I_L and I_F, the energy expenditure E, and the fat mass F. This expression for $f_F E$ can be substituted into the system of differential equations described by equations (2.13) and (2.14) such

that,

$$\rho_F \frac{dF}{dt} = I_F - \left(\frac{A\frac{\rho_L}{\rho_F}\frac{I_F}{F} - I_L + E}{1 + A\frac{\rho_L}{\rho_F}\frac{1}{F}} \right), \tag{4.4}$$

$$\rho_L \frac{dL}{dt} = I_L - E + \left(\frac{A\frac{\rho_L}{\rho_F}\frac{I_F}{F} - I_L + E}{1 + A\frac{\rho_L}{\rho_F}\frac{1}{F}} \right). \tag{4.5}$$

By determining A for different genders and ethnicity, we effectively incorporate gender and ethnicity into the existing model for fat and lean mass change.

As stated above, the value of A is determined by fitting equation (4.1) to the body composition data, collected by Lear *et al.* [20]. We do this by a least squares method [28]. First, we separate the data, according to ethnicity and gender, into the eight groups described in Chapter 3. Next, we determine the average L and F values for each group. Then, we assume that L is a linear function with respect to $\ln F$ and complete a linear regression analysis to determine the best-fit line, corresponding to the best estimate of the parameters A and B, along with their associated uncertainties [28]. Finally, we can test the 'goodness of fit' of our regression line by calculating the correlation number r and the coefficient of determination R^2 [28] using a least squares technique. This technique is used to minimize the sum of squares of the vertical distances between each data point and the corresponding point on the regression line. The minimum value for this sum results in a line of best fit. By using the least squares technique we are assuming that the residuals (the error) have normal distribution and that the residuals also have equal variance. This fit are summarized in Table 4.1.

	European	Aboriginal	Chinese	South Asian
		women		
A	8.174 ± 1.526	10.314 ± 1.693	7.579 ± 1.306	8.068 ± 1.363
B	17.1139	8.54751	16.0079	12.432
R^2	0.224822	0.274685	0.222115	0.257548
		men		
A	9.510 ± 1.920	8.412 ± 2.368	11.641 ± 1.756	5.49 ± 1.86
B	36.1822	35.3531	22.7256	40.88
R^2	0.19852	0.118354	0.305285	0.079

Table 4.1: Fit parameters for function $L = A\text{Ln}F + B$ and corresponding R^2 values for women and men.

In Figure 4.3, we plot the Forbes curves (4.1) for the different ethnic/gender groups, using the parameter values from Table 4.1. We now can compare predictions about fat and lean mass change for each group. If we examine the

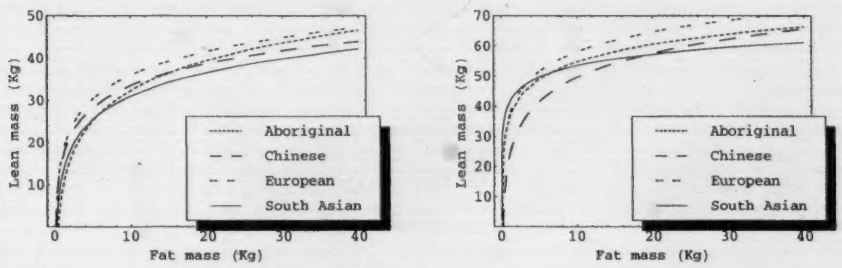


Figure 4.2: Forbes curves for (a) women, and (b) men. These curves correspond to function $L = A\text{ln}F + B$, where A and B are taken from Table 4.1.

Forbes curves at low values of fat mass, we can make the observation that for a fixed weight change in women, individuals from both Chinese and European populations will lose (or gain) more weight in the form of lean mass, as compared to both the Aboriginal and South Asian women. For male populations, at low values of fat mass, we can make a similar observation. In this case, for a fixed weight change, the South Asian men will lose (or gain) more weight in the form of lean mass, as compared to all other male groups. Also, the Chinese men will lose (or gain) the least amount of lean mass for a fixed weight change,

as compared to all other groups.

The reliability of these predictions depend on the accuracy of the Forbes parameter A. From Table 4.1, we see that the R^2 values for each fit (excluding the South Asian men) are small ($0.12 < R^2 < 0.31$). Here, the R^2 value for the South Asian men is very small ($R^2 = 0.079$) and statistically insignificant. These small values for R^2 indicate that the model of the Forbes curve explains less than 31 percent of the variability in the data for all groups and, as a result, this model does not describe the data well. Here, we determine that another model may be more useful. In the next section, we introduce a new variable for height into the model of Forbes curve and determine that a better fit does exist.

4.2 Height as a Determinant of Lean Mass

It has been suggested that height plays a role in determining body composition. In a previous study, Forbes found that lean mass was related to height for all ages of men [9]. He also found that the correlation of this relationship, as determined by the regression coefficient r, is greatest for men between the ages of 10 and 50, and that during this time period, height has a greater effect on lean mass in males than in females. However, during the first 10 years of life, and after the age of 50, he found that the correlation was similar for both genders. For individuals of all ages and both genders, he discovered that most r values were statistically significant. Thus, he concluded that height should be taken into account when comparing lean data in various groups. Here, we modify equation (4.1) to include height H, namely

$$L = A\ln F + B + CH, \tag{4.6}$$

where C (like A and B) is an unknown parameter to be determined. By fitting equation (4.6) to height H, as well as body composition (L and F), it is likely that we will determine a better fit after completion of a linear

	European	Aboriginal	Chinese	South Asian
		women		
A	7.618 ± 1.319	9.684 ± 1.376	6.528 ± 1.143	7.556 ± 1.249
B	-64.907	-72.017	-43.887	-44.087
C	50.840	9.685	40.095	36.420
R^2	0.430	0.521	0.421	0.388
		men		
A	8.985 ± 1.731	7.183 ± 1.935	7.620 ± 1.448	5.59 ± 1.46667
B	-72.990	-103.472	-77.922	-76.708
C	62.300	82.180	66.257	67.628
R^2	0.357	0.422	0.586	0.433

Table 4.2: Fit Parameters for function $L = A\text{Ln}F + B + CH$ and R^2 values for women and men.

regression analysis. That is, we are likely to determine a fit having higher r and R^2 values.

We then perform a multivariate linear regression analysis to determine parameters A, B, and C [28], along with their associated uncertainties. It is important to note that the addition of the CH term changes the value of the Forbes parameter A during the fitting process. It is also important to note that the parameter B, and the addition of the CH term, does not change the general differential form of Forbes equation (4.2). The results of the multivariate linear regression analysis are summarized in Table 4.2. Note that the R^2 values are significantly larger than before ($0.36 < R^2 < 0.59$) for all groups, indicating that this new model fits the data much better. In future calculations, we use the values for the Forbes parameter A from Table 4.2.

4.3 Energy Expenditure Function

Previously, in Chapter 2, the energy expenditure E was described using direct measurements. That is, the total energy expenditure was clinically measured, over a given interval of time, and recorded. The recorded values were then interpolated, and the interpolated energy function was numerically integrated.

Here, to reduce the amount of model input, we discuss an alternate way of describing this energy function. In particular, we will write E in terms of F, L, and the model input I_T. By doing this, we will be able to calculate E without taking any clinical measurements.

Reasons for why we express the energy expenditure in this way comes from the fact that, in recent years, energy expenditure has been described as a function of body composition, specifically lean and fat mass [6]. Studies have concluded that there is a definite linear correlation between resting energy expenditure and lean mass. Also, many studies predict that lean mass is positively correlated with total energy expenditure. However, an independent contribution of fat mass has not been shown to predict resting energy expenditure or total energy expenditure very well in normal weight populations. Although, it is believed that this contribution may be more important for obese individuals, specifically women.

Recall, from Chapter 2, that the total energy expenditure E is equal to the sum of the resting energy expenditure REE, the physical activity PA, and the thermal effect of feeding TEF. Here, we describe the components of the energy expenditure as

$$REE = \alpha + \beta L + \gamma F, \tag{4.7}$$

$$PA = \xi(F + L), \tag{4.8}$$

$$TEF = \sigma I_T, \tag{4.9}$$

so that

$$E(F, L; I_T) = \alpha + \beta L + \gamma F + \xi(F + L) + \sigma I_T \tag{4.10}$$

is a linear multivariate function of lean mass (L), fat mass (F), total body weight ($F + L$), and the total intake rate of food (I_T).

A similar expression for REE has been used by Cunningham [6], where parameters have been found to have the approximate values of $\alpha = 460 \frac{\text{Kcal}}{\text{day}}$, β

$= 19.9 \frac{\text{Kcal}}{\text{Kg·day}}$, and $\gamma = 2.6 \frac{\text{Kcal}}{\text{Kg·day}}$. We will fix these parameter values in future implementation of our model.

Also, similar expressions for PA and TEF have been used by Hall in recent studies [12]. Here, we fix $\sigma = 0.1$. That is, we assume that approximately 10 percent of TEF is due to the total intake rate of food I_T [35].

The parameter ξ is ehtnic/gender specific and is determined from initial data, where initially, individuals are at a steady state, meaning that there is no change in their total body weight. At steady state, $E(F, L; I_T) = I_T$ and ξ is determined by substituting the average baseline feeding measurement (the initial I_T) and the average initial fat and lean mass measurements (F_i and L_i) for each ethnic/gender group into equation (4.10) and solving for ξ such that

$$\xi_i = \frac{(1-\sigma)I_T - \alpha - (\beta F_i + \gamma L_i)}{F_i + L_i}. \tag{4.11}$$

This is not the standard way of representing the PA. In general, PA is calculated as the ratio of the total energy expenditure E to the resting energy expenditure REE [8]. If PA is less than 1.4, then the individual is considered to lead a sedentary lifestyle; if $1.4 \leq PA \leq 1.6$, then the individual in considered inactive; if $1.6 \leq PA \leq 1.9$, then the individual is considered active; and if $PA \geq 1.9$, then the individual is considered to be extremely active. Calculated values for PA are summarized in Tables 5.1 to 5.8. Also, the values used for F_i, L_i, and I_T can be found in Tables 5.1 to 5.8.

We can incorporate the new expression for energy expenditure into our model by substituting equation (4.10) back into the ODE model described by equations (4.4) and (4.5) such that

$$\rho_F \frac{dF}{dt} = I_F - \left(\frac{A\frac{\rho_L}{\rho_F}\frac{I_E}{F} - I_L + E(F, L; I_T)}{1 + A\frac{\rho_L}{\rho_F}\frac{1}{F}} \right), \tag{4.12}$$

$$\rho_L \frac{dL}{dt} = I_L - E(F, L; I_T) + \left(\frac{A\frac{\rho_L}{\rho_F}\frac{I_E}{F} - I_L + E(F, L; I_T)}{1 + A\frac{\rho_L}{\rho_F}\frac{1}{F}} \right). \tag{4.13}$$

To test how well our new energy expenditure might predict body composition

change, we reworked the calculations for determining F and L using the same initial data from the Diaz study (the original calculation was completed in Section (2.2)). Instead of using the interpolated energy expenditure function as shown in Figure 2.2, we used the functional form described by equation (4.10). Here, we noticed similar trajectories for F and L, as compared to those in Figure 2.4.

From the model described by equations (4.12) and 4.13), it is important to note that the intake rates I_L and I_F are kept constant, meaning that the model is autonomous. We also note that changes in F and L do not depend on the separate intake rates, I_F and I_L. Changes in body composition are described only by the total intake rate I_T. The derivation is as follows:

$$\begin{aligned}
\rho_F \frac{dF}{dt} &= I_F - \left[\frac{\frac{I_F A \rho_L}{F \rho_F} - I_L + E(F, L; I_T)}{1 + \frac{A\rho_L}{F\rho_F}}\right] \\
&= \frac{I_F(1 + \frac{A\rho_L}{F\rho_F}) - \frac{I_F A \rho_L}{F\rho_F} + I_L - E(F, L; I_T)}{1 + \frac{A\rho_L}{F\rho_F}} \\
&= \frac{I_F + I_L - E(F, L; I_T)}{1 + \frac{A\rho_L}{F\rho_F}} \\
&= \frac{I_T - E(F, L; I_T)}{1 + \frac{A\rho_L}{F\rho_F}},
\end{aligned}$$

where E depends on I_T and not on the individual intake rates. Similarly, we rewrite equation (4.13) as follows:

$$\rho_L \frac{dL}{dt} = I_L + [\frac{\frac{I_F A\rho_L}{F\rho_F} - I_L + E(F,L;I_T)}{1+\frac{A\rho_L}{F\rho_F}}] - E(F,L;I_T)$$
$$= \frac{I_L(1+\frac{A\rho_L}{F\rho_F}) + \frac{I_F A\rho_L}{F\rho_F} - I_L + E(F,L;I_T) - (1+\frac{A\rho_L}{F\rho_F})E(F,L;I_T)}{1+\frac{A\rho_L}{F\rho_F}}$$
$$= \frac{\frac{A\rho_L}{F\rho_F}(I_T - E(F,L;I_T))}{1+\frac{A\rho_L}{F\rho_F}}.$$

The fact that changes in F and L do not depend on the separate intake rates is an important property of the model. Many nutritionists like the simplicity of this property and like to think of 'a calorie as a calorie'. This means that regardless of the macronutrient composition of the diet, the body weight, body composition, and rate of change of body weight depend only on the energy balance/imbalance between that which is absorbed as food and that which is expended. This is the opinion of the majority of researchers in the field. We have neglected the fact that individual changes in body composition may depend on the proportion of fat and lean mass an individual consumes. This is due to the fact that fat and lean mass are metabolized at different rates [18]. That is, there is a so-called hierarchy between the oxidation rates. Recall, from equation (4.3), that when the nonfat intake rate, I_L, is fixed, wide variations in fat intake rate, I_F, have little impact on the fat oxidation rate, $f_F E$. However, when I_F is fixed, alterations in I_L create a significant change in $f_F E$. Due to the different rates of oxidation, it may be important to describe the thermic effect of feeding as

$$TEF = \delta I_L + \eta I_F, \tag{4.14}$$

where $\eta < \delta$. Recall that the previous expression for TEF is described by equation (4.10), where this energy component depends only on the total intake rate I_T, rather than the separate intake rates I_L and I_F. By substituting equation

(4.14) into the model described by equations (4.12) and (4.13), changes in lean and fat mass would depend on the amount of lean and fat mass consumed. For simplicity, we do not explore this idea further. However, the idea is interesting and has been examined in previous studies by Hall [12].

4.4 Extension of Model to Account for VAT

In recent studies by Hall and Hallgreen [15], it has been shown that there exists a mathematical relationship between changes in total fat mass F and total visceral adipose tissue VAT. Hall *et al.* hypothesized that changes of VAT mass are allometrically related to changes of total fat mass, regardless of the type of weight loss intervention.

In order to test this hypothesis and to determine a relationship between VAT and total fat mass, Hall *et al.* first completed an extensive literature search of published data on VAT and total fat mass measurements during weight loss, where the data had to satisfy certain criteria. That is, that total fat mass was to be measured using either DEXA Scans, underwater weighing, whole body CT scanning, magnetic resonance imaging (MRI), or air displacement plethysmography [35]. Also, VAT had to be measured using MRI or CT imaging. The literature search by Hall *et al.* successfully resulted in finding 37 weight loss intervention studies, representing 1407 subjects. The total population consisted of 24 percent men and 73 percent women (24 percent of which were postmenopausal). The types of weight loss interventions included caloric restriction, endurance exercise, resistance exercise, and bariatric surgery.

Hall *et al.* next hypothesized that changes in VAT and fat mass could be described by the following differential equation,

$$\frac{dVAT}{dF} = k\frac{VAT}{F}. \tag{4.15}$$

where k is an unknown parameter to be determined. This type of equation was used since it has a rich history in the biological sciences and was first used

by Huxley to describe the law of constant differential growth between various body parts of an organism [16]. This hypothesis requires that the ratio of the change of VAT to a change of fat mass, $\Delta VAT/\Delta F$, is proportional to the initial ratio of VAT to fat mass. Using the reported data, Hall *et al.* calculated these ratios and determined that the best fit value of k is 1.3 ± 0.1 with $R^2 = 0.73$, indicating that the model explained more than 70 percent of the variability in the reported data. This value of k was found to adequately describe both genders as well as a variety of weight loss interventions. Hall states that this result suggests that differences in men and women can be explained by the initial VAT and F ratio and that there is no preferential benefit of one weight loss intervention over another.

By integration of equation (4.15), we obtain the power law

$$VAT = bF^k, \tag{4.16}$$

where b is a parameter found from baseline VAT measurements and initial fat measurements. Recall, from the study by Lear *et al.* [20], that VAT is measured using CT-scanning techniques. This means that only single-slice areas of VAT can be measured. In order to write VAT measurements in terms of volume (to piece all the slices together), an equation determined by Shen *et al.* is used [30]. These measurements can then be converted to mass measurements. Initial measurements for VAT and fat mass are taken from Lear *et al.*'s data set described in Chapter 3 and are averaged for each ethnic/gender group. The average values are then substituted into equation (4.16) to determine values for the parameter b. This parameter will not be a constant, but will depend on the gender, ethnicity, and other potential factors that contribute to determining initial VAT. Values for this parameter are recorded in Tables 5.1 to 5.8.

Recall that these results are based on data from weight loss studies only. Therefore, whether these results can be used for weight gain studies is questionable. However, Hall *et al.* did complete a similar analysis using data found from two weight gain studies, and found that $k = 1.3$ sufficed. These results

leave us to believe that a similar relationship does exist for weight gain. However, future studies should be completed to investigate this more thoroughly.

Now that we have an expression to describe VAT in terms of fat mass, we have completed the extension of our model. First we solve for lean and fat mass, by numerically integrating for $L(t)$ and $F(t)$ in equations (4.12) and (4.13) (where these functions, as described in Section (4.2), will depend on ethnicity and gender). We can then describe how VAT mass changes over time by substituting the solution for $F(t)$ into equation (4.16) and numerically solving for $VAT(t)$.

4.5 Analysis of the New Model

In this section, we take a closer look at the mathematics of the model described in Section 4.3. We begin by determining the local behavior about steady-state solutions for the system described by equations (4.12) and (4.13). Next, using fundamental ODE theory, we extend our analysis to describe the global behavior of this system.

Determination of Steady-state Solutions

By setting dF/dt and dL/dt in equations (4.12) and (4.13) equal to zero, we are able to determine the steady-state solutions of our model. It is clear that at steady state, $E = I_T$. This implies that in order for an individual to stay at a constant weight (constant F and L), the individual must expend the same amount of energy as he/she consumes. If we substitute the expression for E, described by equation (4.10), into the expression for the steady state, $E = I_T$, we can solve for L in terms of F, namely

$$L = \frac{(1-\sigma)I_T - \alpha}{\beta + \xi} - \frac{\gamma + \xi}{\beta + \xi} F. \tag{4.17}$$

From this it is clear that, at steady state, our system is characterized by a line of steady states,

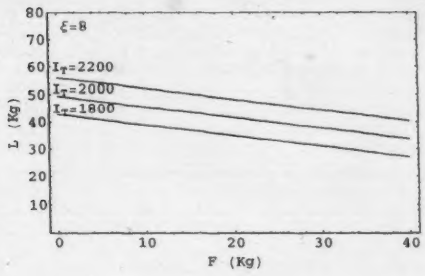


Figure 4.3: Shift of the nullcline from baseline feeding (I_T = 2000 Kcal/day) for both overfeeding (I_T = 2200 Kcal/day) and underfeeding (I_T = 1800 Kcal/day).

$$(F^*,L^*) = (F^*, \tfrac{(1-\sigma)I_T-\alpha}{\beta+\xi} - \tfrac{\gamma+\xi}{\beta+\xi}F^*),$$

where $F^* > 0$. This line also corresponds to the nullcline of the system. It intersects the L-axis at $L_{int} = \frac{(1-\sigma)I_T-\alpha}{\beta+\xi}$, and has a slope of $m = -\frac{\gamma+\xi}{\beta+\xi}$, as shown in Figure 4.3. For each line of steady states, the parameters in equation (4.17) have a positive value (as described in Section 4.3). The input parameter I_T is either increased or decreased from its baseline value. From Figure 4.3, we see that an increase or decrease in I_T results in an increase or decrease in L_{int} respectively, while the slope of the nullcline remains fixed.

Proof for Uniqueness of Solutions

To prove uniqueness of solutions we use the Fundamental Existence-Uniqueness Theorem

Theorem 4.5.1. *Let Ω be an open subset of $\mathbf{R}^n$ containing the equilibrium $\mathbf{x}_0$ and assume that $\mathbf{G} \in C^1(\Omega)$. Then there exists an $a > 0$ such that the initial value problem*

$$\dot{\mathbf{x}} = \mathbf{G}(\mathbf{x})$$
$$\mathbf{x}(0) = \mathbf{x}_0$$

has a unique solution $\mathbf{x}(t)$ on the interval $[-a,a]$.

We consider Ω to be the space of all vectors $\begin{pmatrix} F \\ L \end{pmatrix} \in \mathrm{R}^+ \times \mathrm{R}^+ \ / \ \mathbf{0}$ and show that $\mathbf{G} \in C^1(F, L)$, where $\mathbf{G}(F, L) = \begin{pmatrix} g_1(F, L) \\ g_2(F, L) \end{pmatrix} = \begin{pmatrix} \frac{dF}{dt} \\ \frac{dL}{dt} \end{pmatrix}$.

Here,

$$g_1(F, L) = \frac{1}{\rho_F} \left(\frac{I_T(1-\sigma) - (\alpha + \beta L + \gamma F + \xi(F+L))}{1 + \frac{A\rho_L}{F\rho_F}} \right),$$
$$g_2(F, L) = \frac{1}{\rho_L} \left(\frac{A\rho_L}{\rho_F} \frac{(I_T(1-\sigma) - (\alpha + \beta L + \gamma F + \xi(F+L)))}{F + \frac{A\rho_L}{\rho_F}} \right).$$

Letting $\tilde{a} = (1-\sigma)I_T - \alpha$, $\tilde{b} = \beta + \xi$, $\tilde{c} = \gamma + \xi$, $\tilde{d} = \rho_F$, and $\tilde{e} = A\rho_L$, where $\tilde{a}$, $\tilde{b}$, $\tilde{c}$, $\tilde{d}$, and $\tilde{e}$ are constants, we can rewrite g_1 and g_2 as,

$$g_1(F, L) = \frac{\tilde{a} - \tilde{b}L - \tilde{c}F}{\tilde{d} + \frac{\tilde{e}}{F}},$$
$$g_2(F, L) = A\frac{\tilde{a} - \tilde{b}L - \tilde{c}F}{\tilde{d}F + \tilde{e}}.$$

Hence:

$$\frac{dg_1(F, L)}{dF} = \frac{\tilde{c}\left(\tilde{d} + \frac{\tilde{e}}{F}\right) - \left(\frac{-\tilde{e}}{F^2}\right)(\tilde{a} - \tilde{b}L - \tilde{c}F)}{\left(\tilde{d} + \frac{\tilde{e}}{F}\right)^2}$$
$$\frac{dg_1(F, L)}{dL} = \frac{-\tilde{b}}{\tilde{d} + \frac{\tilde{e}}{F}}$$
$$\frac{dg_2(F, L)}{dF} = \frac{A\tilde{c}(\tilde{d}F + \tilde{e}) + \tilde{d}A(\tilde{a} - \tilde{b}L - \tilde{c}F)}{(\tilde{d}F + \tilde{e})^2}$$
$$\frac{dg_2(F, L)}{dL} = \frac{-\tilde{b}}{\tilde{d}F + \tilde{e}}.$$

All partial derivatives are continuous in Ω, as Ω does not contain $F = 0$.

Determination of Stable and Center Subspaces

We have already determined that there are infinitely many steady states. Next, we must examine the stability of these steady states. We start by considering the local behavior of solutions near each steady state using linearization techniques. First we rewrite equations (4.12) and (4.13) in vector notation such that

$$\begin{pmatrix} \frac{dF}{dt} \\ \frac{dL}{dt} \end{pmatrix} = \mathbf{G}(F, L),$$

where again we have

$$\mathbf{G}(F, L) = \begin{pmatrix} g_1(F, L) \\ g_2(F, L) \end{pmatrix}$$

and

$$g_1(F, L) = \frac{1}{\rho_F}\left(\frac{I_T(1-\sigma) - (\alpha + \beta L + \gamma F + \xi(F+L))}{1 + \frac{A\rho_L}{F\rho_F}}\right),$$
$$g_2(F, L) = \frac{1}{\rho_L}\left(\frac{A\rho_L}{\rho_F}\frac{(I_T(1-\sigma) - (\alpha + \beta L + \gamma F + \xi(F+L)))}{F + \frac{A\rho_L}{\rho_F}}\right).$$

The Jacobian Matrix $\mathbf{J}$ for the system described by vector $\mathbf{G}(F, L)$ is

$$\mathbf{J}(F, L) = \mathrm{D}\mathbf{G}(F, L) = \begin{pmatrix} \frac{dg_1(F,L)}{dF} & \frac{dg_1(F,L)}{dL} \\ \frac{dg_2(F,L)}{dF} & \frac{dg_2(F,L)}{dL} \end{pmatrix}.$$

Evaluating $\mathbf{J}$ at the steady state (F^*, L^*), we find that

$$\mathbf{J}_{(F^*,L^*)} = \begin{pmatrix} -\frac{F^*(\gamma+\xi)}{F^*\rho_F + A\rho_L} & -\frac{F^*(\beta+\xi)}{F^*\rho_F + A\rho_L} \\ -\frac{A(\gamma+\xi)}{F^*\rho_F + A\rho_L} & -\frac{A(\beta+\xi)}{F^*\rho_F + A\rho_L} \end{pmatrix}.$$

The eigenvalues for this matrix are given by

$$\lambda_1 = 0,$$
$$\lambda_2 = -\frac{A(\beta+\xi) + F^*(\gamma+\xi)}{F^*\rho_F + A\rho_L}.$$

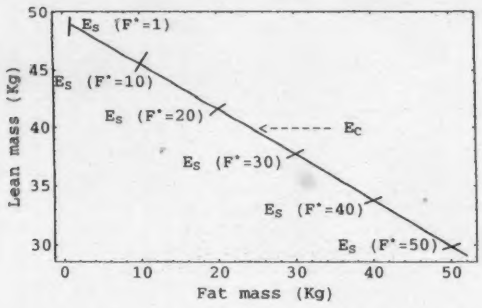


Figure 4.4: Eigenvectors corresponding to E_c and E_s for a finite number of steady states (F^*, L^*).

Since A, ρ_F, ρ_L, β, γ, and ξ are positive, λ_2 is negative for any value of $F^* > 0$. The corresponding eigenvectors are given by

$$\mathbf{V}_{\lambda_1} = \begin{pmatrix} -\frac{\beta+\xi}{\gamma+\xi} \\ 1 \end{pmatrix},$$

$$\mathbf{V}_{\lambda_2} = \begin{pmatrix} \frac{F^*}{A} \\ 1 \end{pmatrix}.$$

Here, $\mathbf{V}_{\lambda_1}$ is defined as the center subspace E_c, corresponding to the zero eigenvalue λ_1, and $\mathbf{V}_{\lambda_2}$ is defined as the stable subspace E_s, corresponding to the negative eigenvalue λ_2. Since $\mathbf{V}_{\lambda_1}$ passes through each equilibrium (F^*, L^*), and has the same slope as the nullcline $(m = -\frac{\gamma+\xi}{\beta+\xi})$, it is clear that E_c coincides with the nullcline. Here $\mathbf{V}_{\lambda_2}$ depends on F^*, such that each eigenvector will have a different slope. As F^* increases, the slope of $\mathbf{V}_{\lambda_2}$ decreases. Figure 4.4 is a plot of E_c and E_s in the (F, L) plane. The eigenvectors corresponding to E_s are calculated for $F^* = 1$, 10, 20, 30, 40, and 50 Kg, where each eigenvector has been scaled to have unit length.

Describing the Stable and Center Manifolds

In the previous section, we have determined the existence of an infinite line of steady states, where the stability of each steady state was tested by exam-

ination of local behavior using linearization methods. It was found that the values of the eigenvalues for each steady state were always zero and negative, respectively. This means that each steady state is nonhyperbolic and that regular stability analysis, such as use of the Hartman Grobman theorem [26], does not apply. However, we did determine the existence of both stable and center subspaces, E_s and E_c, respectively.

We now extend our analysis to determine the global behavior of the system. To do so, we use local center manifold theory. This theory states that the qualitative behavior in the neighborhood of a nonhyperbolic steady state X^* of a nonlinear system with $X^* \in R^n$ is determined by its behavior on the center manifold near X^*. The following is the statement of the Center Manifold Theorem for n-dimensional systems of ODEs [26].

Theorem 4.5.2. *Let* $\mathbf{G} \in C^r(\mathbf{R}^n)$ *and* $r \geq 1$. *Suppose* $\mathbf{G}(\mathbf{0}) = \mathbf{0}$ *and* $D\mathbf{G}(\mathbf{0})$ *has k eigenvalues with negative real part, j eigenvalues with positive real part, and m = n - k - j eigenvalues with zero real part. Then there exists an m-dimensional center manifold* $W^c(\mathbf{0})$ *of class* C^r *tangent to the center subspace* E_c *of the linearized system at* $\mathbf{0}$, *there exists a k-dimensional stable manifold* $W^s(\mathbf{0})$ *of class* C^r *tangent to the stable subspace* E_s *of the linearized system at* $\mathbf{0}$, *and there exists a j-dimensional unstable manifold* $W^u(\mathbf{0})$ *of class* C^r *tangent to the unstable subspace* E_u *of the linearized system at* $\mathbf{0}$; *furthermore,* $W^c(\mathbf{0})$, $W^s(\mathbf{0})$, *and* $W^u(\mathbf{0})$ *are invariant under the flow of the nonlinear system.*

For our system, we have $n = 2$, $k = 1$, $j = 0$, and $m = 1$. Here, we use the fact that both the stable and center manifolds (W^s and W^c) are tangent to their respective stable and center subspaces (E_s and E_c) at each steady state, where we translate each steady state to the origin.

From ODE theory, we know that the stable and center subspaces must not cross paths, except at a steady state. The same is true for both the stable and center manifolds. This fact makes it clear that $W^c = E_c$, as W^c must not cross W^s (and hence must not cross E_s). Here, we numerically compute a

phase portrait corresponding to W^c and W^s in (F, L) space. Recall that, from equation (4.2), $dL/dF = A/F$, thus, integration of both sides of this equation results in the original expression for the Forbes curve (4.1), $L = A\ln F + C_o$, where C_o is a constant of integration to be determined from initial fat and lean mass measurements, F_i and L_i. That is, it is determined by the equation $C_o = L_i - A\ln F_i$, where these values will be calculated in Section 4.6. By letting $A = 10.4$ and choosing different initial values for F_i and L_i, we are able to compute the orbits corresponding to equations (4.12) and (4.13), as shown in Figure 4.5.

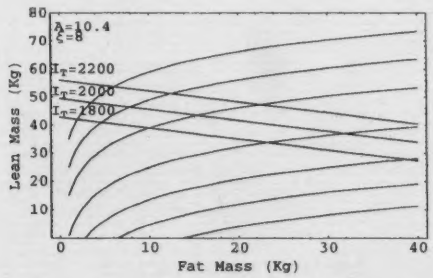


Figure 4.5: Phase portrait for the system of ODEs described by equations (4.12) and (4.13) when $A = 10.4$ and for various initial body compositions.

In this phase portrait, we have included the three different nullclines (or center manifolds) from Figure 4.3, corresponding to baseline feeding, overfeeding, and underfeeding. An important thing to note here is that a change in diet will not have any affect on the orbits of this system; only on the eventual steady state values F^* and L^*. By increasing (or decreasing) I_T, we only increase (or decrease) the height of the nullcline described by equation (4.17), and thereby increase (or decrease) the steady-state values of F^* and L^*. For example, given a fixed caloric decrease in diet, a person will travel downwards along a particular orbit, starting from their initial body composition. The person will continue his/her path through phase space along their Forbes curve until he/she reaches the steady state (F^*, L^*) determined by the intersection of his/her Forbes curve and the center manifold corresponding to his/her caloric intake. If the diet is not changed again, a person will remain at this steady

state. However, if the diet is decreased again (by a fixed amount), the person will travel downwards along the same Forbes curve as before, until he/she reach their next steady state at a lower value of F^* and L^* along another nullcline (corresponding to a lower value I_T). In summary, a person will follow their own unique path through phase space, where this path is dependent on his/her initial body composition. This unique path is described by the Forbes curve (4.1) and hence depends on the individual's corresponding value of the parameter A.

4.6 Production of Forbes Curves for Different Ethnic/Gender Groups

Here, we recall from Section 4.1 that body composition change can be compared (for each ethnic/gender group) by using the Forbes curves shown in Figure 4.2. We also recall that values for the Forbes parameter A and the parameter B are determined by fitting equation (4.1) to body composition data for the different ethnic/gender groups. Here, we found that the correlation coefficients for these initial fits (as described by the R^2 values) were very low. Therefore, it is not likely that these curves accurately describe body composition change.

To increase the correlation of the initial fit, we included height H to equation (4.1) to obtain equation (4.2). The correlation of this fit was found to be much higher than the original fit. Therefore, it is more likely that the new values for the parameter A can be used to more accurately describe body composition change. Recall that the original and new values for the parameter A, along with their corresponding correlation coefficients, are found in Tables 4.1 and 4.2 respectively.

Now, from Section 4.5, it is found that individuals follow their own unique path through phase space, described by the Forbes curve $L = A\ln F + C_o$, where values for the parameter A, for the different gender/ethnic groups, are

those found in Table 4.2. Here, this path not only depends on the parameter A, but also on the individual's initial body composition. Specifically, the parameter C_o is determined from F_i and L_i using the equation $C_o = L_i$ - $A\ln F_i$, where average values of F_i and L_i, for each ethnic/gender group, are found using the fat and lean mass measurements taken from the data set described in Chapter 3. These values, as well as values for C_o, are summarized in Table 4.3. In Figure 4.6, we produce a new set of Forbes curves corresponding to female and male populations respectively. This figure can be compared to the previous Forbes curves shown in Figure 4.2.

Figure 4.6(a) shows that for small values of F and for a fixed weight change in women, the Chinese and European will gain (lose) more weight in the form of lean mass, as compared to Aboriginal and South Asian women. From Figure 4.6(b) we see that, for men, the Forbes curves are more difficult to distinguish for small values of F. This makes it hard to make predictions about fat and lean mass change. However, for higher values of F, we see that the Aboriginal and European men are more lean than the other ethnic groups.

Parameters	European	Aboriginal	Chinese	South Asian
women				
L_i (Kg)	44.56	43.51	39.76	39.55
F_i (Kg)	30.75	31.56	23.95	30.58
C_o (Kg)	18.46	10.08	19.03	13.71
men				
L_i (Kg)	65.07	61.56	56.17	58.21
F_i (Kg)	15.49	15.35	13.96	17.20
C_o (Kg)	37.06	38.52	33.92	40.17

Table 4.3: Values for F_i, L_i, and C_o for all women and men.

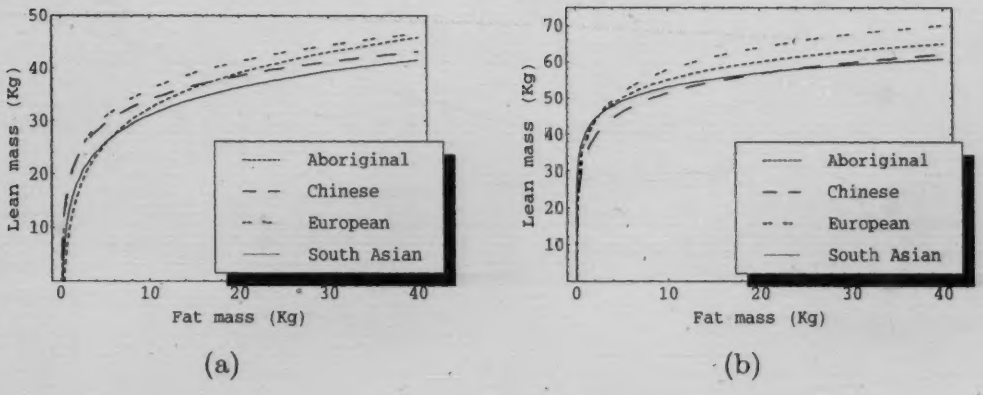


Figure 4.6: Forbes curves for (a) women, and (b) men. These curves correspond to function $L = A\ln F + C_o$, where A and C_o are taken from Table 4.3.

Chapter 5

Results and Discussion

In this chapter, we present the results for simulations completed using the model described in Chapter 4. Here, we obtain numerical solutions for $F(t)$ and $L(t)$ from equations (4.12) and (4.13). From these solutions, we can compute fat and lean mass changes, as well as VAT mass change by implementing equation (4.16). We will carry out simulations in which we increase (and then decrease) the caloric intake, for all groups, from baseline measurements. Recall that the eight ethnic/gender groups discussed in this study include Aboriginal, Chinese, European, and South Asian populations.

First, in Section 5.1, we discuss our model setup. Next, in Section 5.2, we present results of simulations completed when we neglect differences in BMI measurements. Here we have grouped all subjects of the same ethnicity/gender into one cohort, regardless of their BMI, and found average values for the input parameters L_i, F_i, VAT_i, I_T, and b. In Sections 5.3 to 5.5, we further subdivide each cohort according to BMI. Specifically, we separate each ethnic/gender group according to the following three BMI ranges: 18.5 to 24.9 Kg/m^2, 25 to 29.9 Kg/m^2, and $\geq$ 30 Kg/m^2. These ranges correspond to healthy, overweight, and obese individuals respectively. Again, we complete overfeeding (and then underfeeding) simulations. Next, in Section 5.6, we complete a sensitivity analysis to determine how sensitive lean and fat mass are to changes in diet for each group. Finally, in Section 5.7, we give a brief discussion of the chapter

results.

5.1 Model Setup

First, average values for lean, fat, and VAT mass are calculated for each ethnic/gender group, neglecting differences in BMI. These averages are calculated using the data set collected by Lear *et al.* [20] and correspond to the average initial values for lean mass L_i, fat mass F_i, and VAT mass VAT_i respectively. The model inputs described here are summarized in Tables 5.1 and 5.2.

Next, each group is subdivided according to the three BMI ranges described at the beginning of this chapter. New averages for input parameters L_i, F_i, and VAT_i are calculated for these groups and are summarized in Tables 5.3 to 5.8.

Total intake rates I_T are also averaged for each BMI group (using the data set) and correspond to the baseline feeding measurements. Initially, the average intake rates were quite low (for all BMI groups). In many cases, when asked to document caloric intake, individuals tend to underestimate how much they are eating. Studies have suggested that many individuals underestimate their intake rate by an average of 20 % [33]. Therefore, in order to obtain more reasonable intake rates, we increase each group's average baseline intake rate by 20 %. These increased baseline intake rates are recorded in Tables 5.1 to 5.8 and will be used as model input.

Knowing L_i, F_i, and I_T, we are able to compute the value of the parameter ξ by using equation (4.11). These obtained values of ξ are recorded in Tables 5.1 to 5.8.

Also, in Tables 5.1 to 5.8, we record the percentage of fat and lean mass in each groups diet (% I_F and % I_L), as well as the value for the parameter b. Recall, from Section 4.4, that this parameter is calculated from initial VAT and fat mass, so it too depends on ethnicity and gender.

In all simulations, we are able to record lean, fat, and VAT mass over time. At baseline feeding, these masses remain constant for all time. Here we increase

(decrease) each group's baseline intake rates by increments of 100 Kcal/day, up to (down to) and including 500 Kcal/day. We do this to examine differences (if any) in body composition change over time for the different ethnic/gender groups.

Parameters	European	Aboriginal	Chinese	South Asian
women				
L_i (Kg)	44.56	43.51	39.76	39.55
F_i (Kg)	30.75	31.56	23.95	30.58
VAT_i (Kg)	2.18	2.32	1.88	2.12
Baseline I_T (Kcal/day)	2103.67	2038.52	2274.18	1928.97
% I_L	66.45	66.17	66.87	71.57
% I_F	33.55	33.83	33.13	28.43
b	0.025	0.026	0.030	0.025
ξ (Kcal/Kg·day)	6.19	5.68	11.51	5.84

Table 5.1: Averaged model input parameters for all women.

Parameters	European	Aboriginal	Chinese	South Asian
men				
L_i (Kg)	65.07	61.56	56.17	58.21
F_i (Kg)	22.59	24.73	18.54	25.23
VAT_i (Kg)	2.92	3.15	2.65	3.49
Baseline I_T (Kcal/day)	2816.98	2283.22	2616.57	2298.53
% I_L	66.44	65.94	68.29	73.37
% I_F	33.56	34.06	31.71	26.63
b	0.051	0.048	0.060	0.053
ξ (Kcal/Kg·day)	8.23	3.53	9.75	4.61

Table 5.2: Averaged model input parameters for all men.

Parameters	European	Aboriginal	Chinese	South Asian
women				
L_i (Kg)	40.53	38.61	37.03	35.90
F_i (Kg)	19.48	19.97	18.01	21.66
VAT_i (Kg)	1.45	1.30	1.39	1.61
Baseline I_T (Kcal/day)	2112.27	1994.52	2228.33	1959.18
% I_L	67.16	67.18	68.32	70.44
% I_F	32.84	32.82	31.68	29.56
b	0.031	0.026	0.032	0.030
ξ (Kcal/Kg·day)	9.73	8.79	13.82	9.25

Table 5.3: Averaged model input parameters for women of BMI 18.5 to 24.9 Kg/m^2.

Parameters	European	Aboriginal	Chinese	South Asian
men				
L_i (Kg)	50.42	52.64	51.83	53.34
F_i (Kg)	15.49	15.35	13.96	17.20
VAT_i (Kg)	1.68	1.62	1.74	2.17
Baseline I_T (Kcal/day)	2691.76	2353.65	2824.76	2192.87
% I_L	69.10	66.1	69.07	74.63
% I_F	30.90	33.90	30.93	25.37
b	0.048	0.040	0.057	0.054
ξ (Kcal/Kg·day)	10.28	8.40	15.42	5.78

Table 5.4: Averaged model input parameters for men of BMI 18.5 to 24.9 Kg/m^2.

Parameters	European	Aboriginal	Chinese	South Asian
women				
L_i (Kg)	44.72	42.48	40.73	40.24
F_i (Kg)	31.32	29.08	26.08	30.49
VAT_i (Kg)	2.08	2.01	2.10	2.24
Baseline I_T (Kcal/day)	2148.52	2131.13	2288.06	1735.20
% I_L	66.7	66.2	66.44	74.44
% I_F	33.3	33.8	33.56	25.56
b	0.024	0.025	0.030	0.026
ξ (Kcal/Kg·day)	6.61	7.50	10.79	3.13

Table 5.5: Averaged model input parameters for women of BMI 25 to 29.9 Kg/m^2.

Parameters	European	Aboriginal	Chinese	South Asian
men				
L_i (Kg)	65.09	60.09	51.83	53.34
F_i (Kg)	21.82	22.95	20.36	25.74
VAT_i (Kg)	2.46	2.65	2.38	3.01
Baseline I_T (Kcal/day)	2960.91	2294.55	2453.61	2276.57
% I_L	63.82	66.58	67.87	74.36
% I_F	36.19	33.42	32.13	25.74
b	0.045	0.045	0.047	0.044
ξ (Kcal/Kg·day)	9.81	4.21	7.03	4.33

Table 5.6: Averaged model input parameters for men of BMI 25 to 29.9 Kg/m^2.

Parameters	European	Aboriginal	Chinese	South Asian
women				
L_i (Kg)	48.96	48.16	44.91	43.18
F_i (Kg)	42.94	42.57	34.86	41.54
VAT_i (Kg)	3.12	3.38	2.94	2.6
Baseline I_T (Kcal/day)	2039.74	1981.25	2368.65	2120.67
% I_L	65.32	65.40	63.84	69.55
% I_F	34.68	34.60	36.16	30.45
b	0.024	0.026	0.029	0.020
ξ (Kcal/Kg·day)	3.15	2.80	8.62	5.68

Table 5.7: Averaged model input parameters for women of BMI $\geq$ 30 Kg/m^2.

Parameters	European	Aboriginal	Chinese	South Asian
men				
L_i (Kg)	73.18	68.27	65.26	63.80
F_i (Kg)	32.43	32.24	27.02	33.74
VAT_i (Kg)	3.29	3.12	3.03	3.54
Baseline I_T (Kcal/day)	2763.78	2230.56	2574.79	2449.96
% I_L	67.06	64.99	67.33	72.84
% I_F	32.94	35.01	32.67	27.16
b	0.036	0.034	0.042	0.036
ξ (Kcal/Kg·day)	4.55	1.04	5.29	3.97

Table 5.8: Averaged model input parameters for men of BMI $\geq$ 30 Kg/m^2.

5.1.1 Analysis of Initial Model Input

Using Tables 5.1 to 5.8, we can calculate the average initial body weight W_i for each group (i.e., $W_i = F_i + L_i$). From this, we are able to determine the percentage of weight that corresponds to lean mass, fat mass, and VAT mass in each group. This information is important because it gives us a good description of the initial body composition makeup for each group. Specifically, this information will tell us which group is the leanest on average and which group is the least lean on average. These percentages are summarized in Figure 5.1.

From Figure 5.1, we see that there are many interesting similarities between the different gender groups, as well as between the different ethnic groups. We first make the observation that, in general, men are more lean than women. We also observe that populations of the same ethnicity have similar initial body composition makeup. For example, individuals from male and female South Asian populations have a greater percentage of weight in the form of fat mass and a smaller percentage of weight in the form of lean mass, as compared to their respective gender groups. That is, they are the least lean, for all ranges of BMI, as compared to their respective gender groups. Also, in most cases, individuals from the Chinese populations are the leanest. That is, they have a greater percentage of weight in the form of lean mass, and a smaller percentage of weight in the form of fat mass, for almost all ranges of BMI. The only exceptions are women in the healthy BMI range and men in the overweight BMI range. In both of these cases it is the Europeans who are initially the leanest.

Initial VAT mass differs among all ethnic/gender groups. For the case when all women are grouped together and for women in the obese BMI range, the Aboriginal females have the greatest percentage of weight in the form of VAT mass, as compared to all other female groups. For women in the healthy and overweight BMI ranges, it is the South Asian women who initially have the greatest percentage of weight in the form of VAT mass. For all BMI ranges,

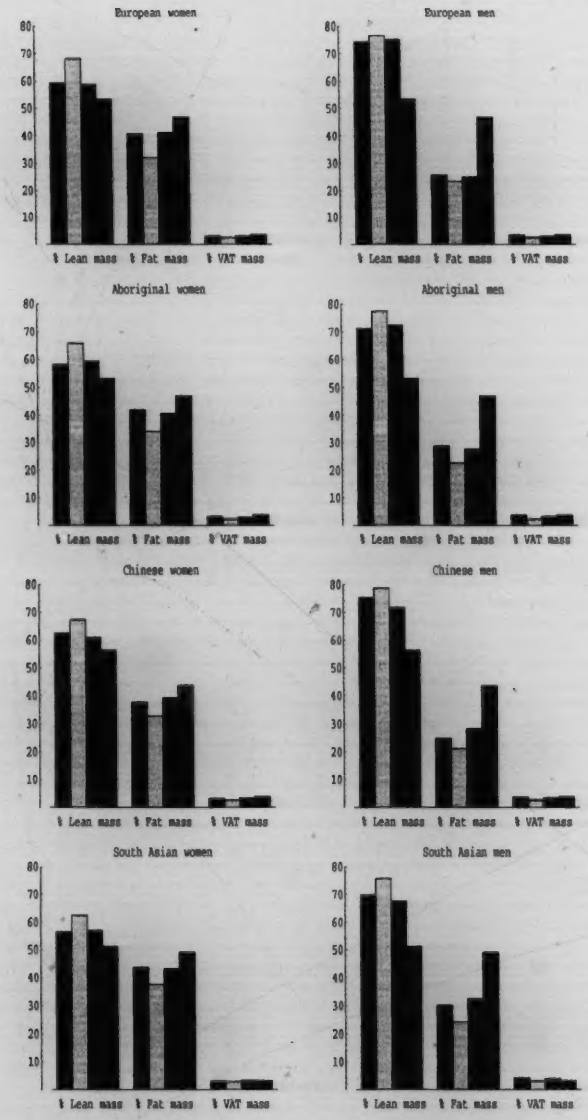


Figure 5.1: Initial percentage of body weight corresponding to lean, fat, and VAT mass for women and men. The red bar represents initial percentages for all men and women, the yellow bar represents healthy individuals, the teal bar represents overweight individuals, and the blue bar represents obese individuals.

South Asian males have the greatest percentage of weight in the form of VAT mass, as compared to all other male groups.

For the case when all individuals are grouped together and for individuals in the obese BMI range, both male and female European populations have the least amount of weight in the form of VAT mass, as compared to their respective gender groups. Females and males from the Aboriginal populations in the healthy and overweight BMI ranges have the least amount of weight in the form of VAT mass.

Also, it is interesting to note that initial VAT mass percentages are higher for individuals from South Asian populations with a BMI between 24.5 to 29.9 Kg/m^2 than individuals with a BMI $\geq$ 30 Kg/m^2 in these populations. For all other groups, initial VAT mass percentages increase with increasing BMI.

5.2 Weight Change Results

Here we present results for weight change over a time of 5 years for various increases (and decreases) in baseline intake rate for each group. As stated before, we increase (and decrease) each groups diet by increments of 100 Kcal/day up to and including 500 Kcal/day. In addition to presenting the weight change results in terms of absolute changes, we normalize the results so that they can be described in terms of percent changes. We do this in order to better understand how our initial conditions affect the outcome of weight gain and weight loss between the different groups.

We define a relative change in a variable x as $\triangle x/x$, where $\triangle x$ represents a small change in the variable x. The percent change is found by multiplying the relative change by 100. For example, we describe the relative change in L as $\frac{\Delta L}{L_i}$ and the relative change in I_T as $\frac{\Delta I_T}{I_{T_{baseline}}}$ (here we are looking at the relative change in L with respect to the initial lean mass and a relative change in I_T with respect to the initial intake rate).

5.2.1 Case 1: Neglecting Differences in BMI

Figures 5.2 and 5.3 correspond to the results of overfeeding and underfeeding simulations for all women and men respectively. The first two rows of graphs correspond to weight gain and weight loss results, and the last two rows describe the corresponding percent (or relative) changes. That is, they describe mass change relative to initial mass and intake rate change relative to initial diet (the baseline intake rate). The results do not necessarily correspond to solutions at steady state, rather they correspond to results recorded at a time of 5 years.

From the first two rows of figures in Figure 5.2, we see that women from Chinese populations are affected the least by changes in diet. This in seen by the small gains (and losses) in lean, fat, and VAT mass during overfeeding (underfeeding). Here, Aboriginal women are highly affected by changes in diet. That is, they gain (lose) the most amount of lean mass. All populations (excluding the Chinese) gain (lose) similar amounts of fat and VAT mass.

From the last two rows of figures in Figure 5.2, we draw similar conclusions. Relative to their initial body composition and diet, the Chinese women still gain the least percentage of lean mass relative to their initial lean mass, and the Aboriginal women gain the greatest percentage of lean mass, relative to their initial lean mass.

From the first two rows of the figures, it is clear that the Chinese are gaining (losing) the least amount of fat and VAT. However, relative to their initial body composition and initial diet, they are gaining similar percentages as the other groups. This is due to the fact that they initially eat more than all other groups, and that they initially have the smallest fat and VAT mass compositions. Increasing the diet has the effect of decreasing the percent change in diet, and decreasing the initial mass has the effect of increasing the percent change in mass.

From the first two rows of figures of Figure 5.3, we see that the Chinese men are least affected by changes in diet. However, the weight change results

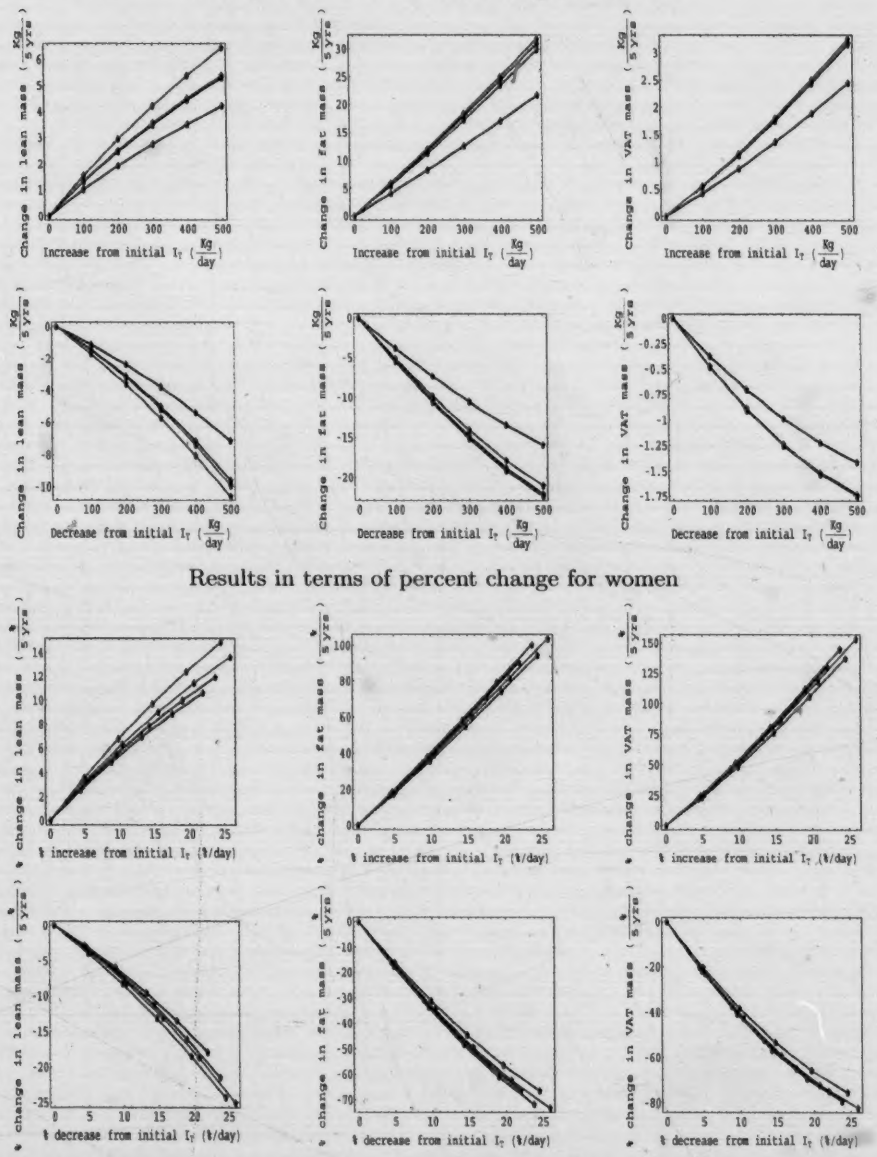

Results in terms of absolute change for women
Change in lean mass (Kg / 5 yrs)
Change in fat mass (Kg / 5 yrs)
Change in VAT mass (Kg / 5 yrs)
Increase from initial I_T (Kg / day)
Decrease from initial I_T (Kg / day)
Results in terms of percent change for women
% change in lean mass (% / 5 yrs)
% change in fat mass (% / 5 yrs)
% change in VAT mass (% / 5 yrs)
% increase from initial I_T (%/day)
% decrease from initial I_T (%/day)

Figure 5.2: Mass change for women as a function of changing diet (change from baseline). Europeans are represented by the red curves, Aboriginal by green, Chinese by blue, and South Asian by purple.

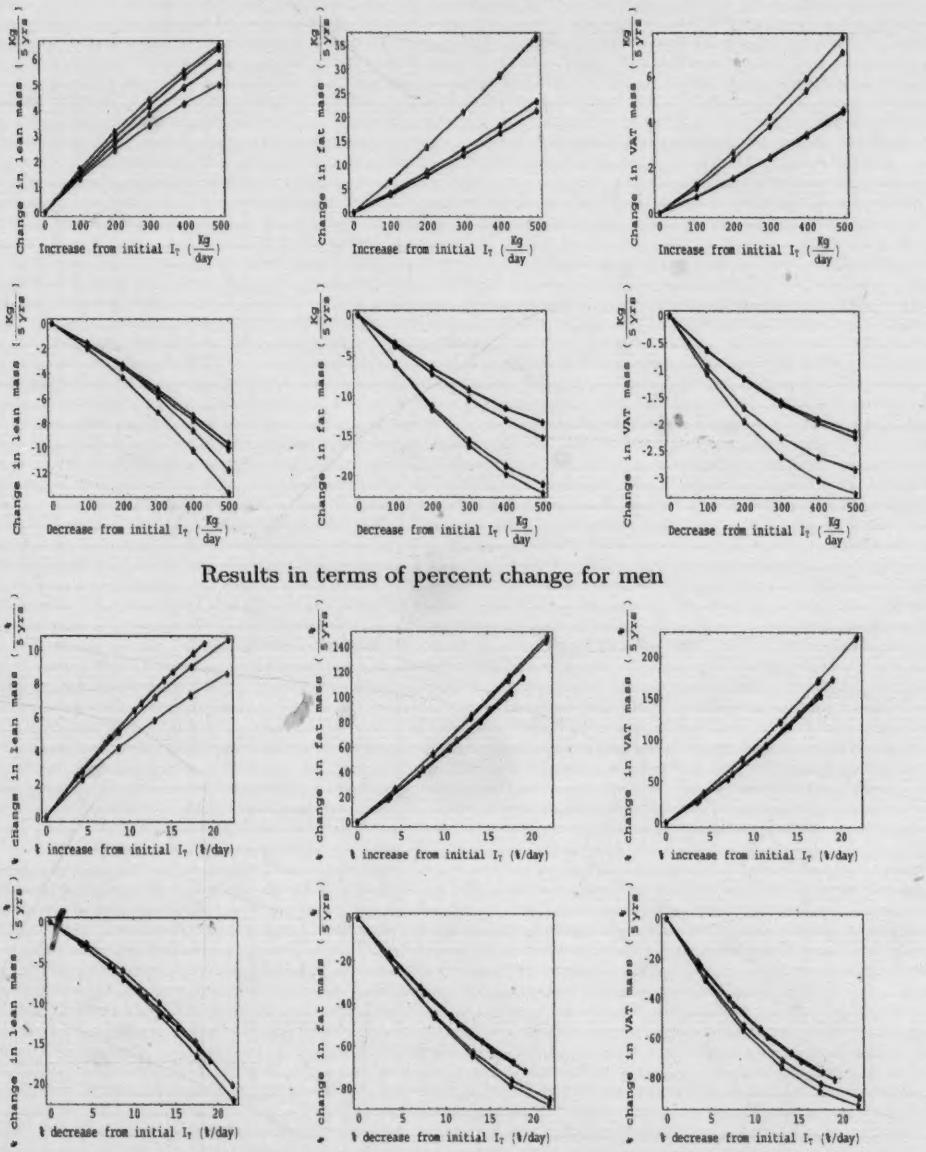

Results in terms of absolute change for men
Change in lean mass (Kg / 5 yrs)
Change in fat mass (Kg / 5 yrs)
Change in VAT mass (Kg / 5 yrs)
Increase from initial I_T (Kg / day)
Decrease from initial I_T (Kg / day)
Results in terms of percent change for men
% change in lean mass (% / 5 yrs)
% change in fat mass (% / 5 yrs)
% change in VAT mass (% / 5 yrs)
% increase from initial I_T (%/day)
% decrease from initial I_T (%/day)

Figure 5.3: Mass change for men as a function of changing diet (change from baseline). Europeans are represented by the red curves, Aboriginal by green, Chinese by blue, and South Asian by purple.

for each type of mass do not vary across the ethnic groups as much for men as they do for women (the curves are closer together). Here, the Chinese men gain (lose) similar amounts of fat and VAT mass, as well as lose a similar amount of lean mass, as the Europeans. Again, the Aboriginal men lose (and gain) the most amount of lean mass, and gain a similar amount of fat mass as the South Asian men. The South Asian men gain (lose) the most VAT mass and gain (lose) the least amount of lean mass.

From the last two rows of Figure 5.3, we see that, relative to their initial body composition, the South Asian men gain the least percentage of lean mass and the Aboriginal men lose the greatest percentage of lean mass. We also see that the South Asian and Aboriginal men gain (lose) a similar percentage of fat and VAT mass and that the European and Chinese men gain (lose) a similar percentage of fat and VAT mass.

5.2.2 Case 2: BMI Range 18.5 to 24.9 Kg/m^2

Figures 5.4 and 5.5 represent weight change results for individuals who are at a healthy weight, according to BMI measurements (that is, individuals having a BMI of 18.5 to 24.9 Kg/m^2).

From Figure 5.4, we see that the results here are qualitatively similar to those of case 1. Here, Chinese women are affected the least by changes in diet, since they gain (lose) the least amount of lean and fat mass. Both the Chinese and Aboriginal women gain the least amount of VAT mass. It is also the case that the Aboriginal and South Asian women are affected the most by changes in diet. The Aboriginal women gain (lose) the most amount of lean mass and the South Asian women gain (lose) the most amount of fat and VAT mass.

In terms of percent changes, the conclusions are similar. It is the Chinese who are gaining the least percentage of lean mass and the Aboriginal who are gaining the most percentage of lean mass, with respect to their initial lean mass. Percent changes for lean and fat mass show that all groups are gaining (and losing) similar percentages of fat and VAT mass, with respect to their

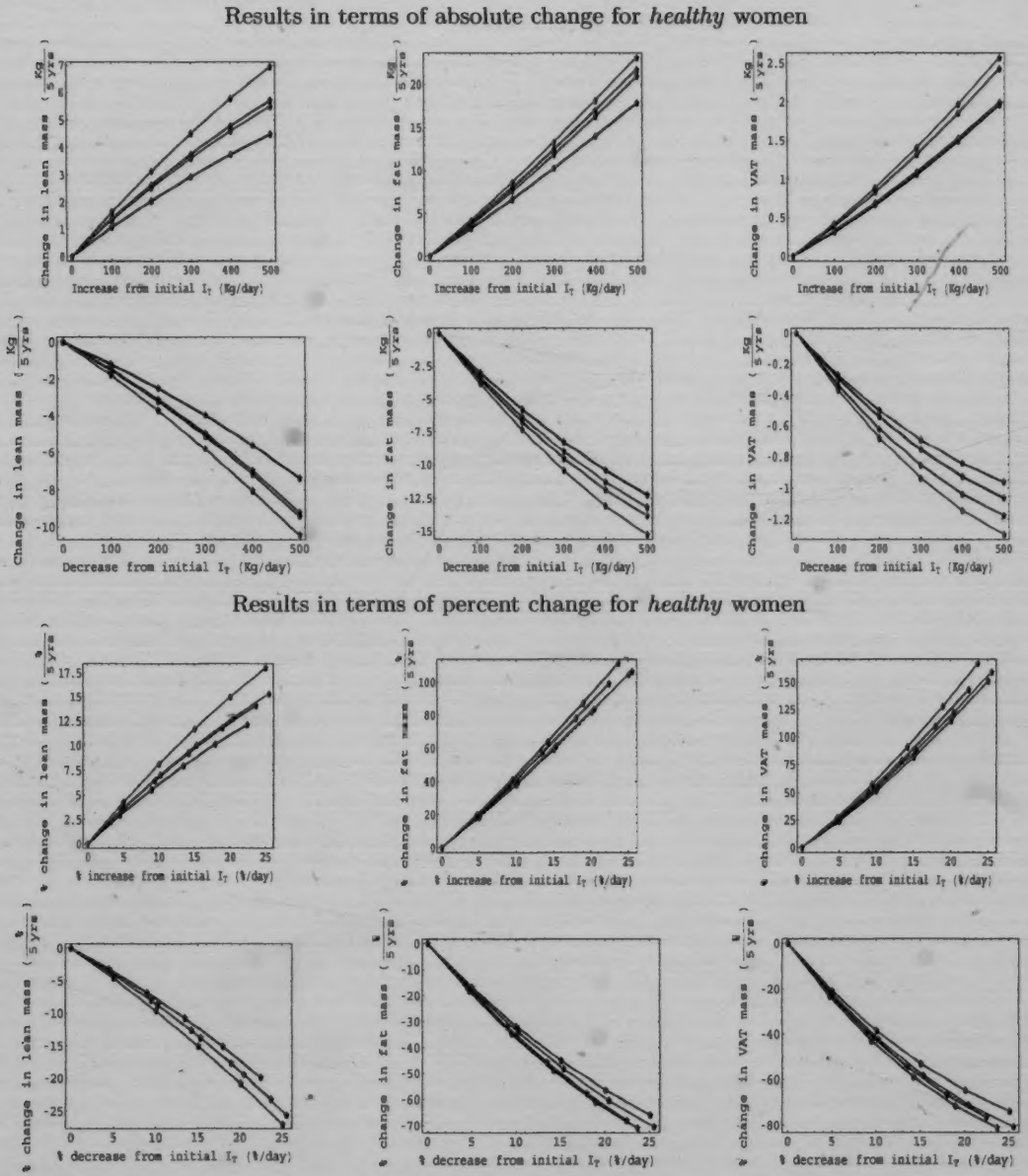

Results in terms of absolute change for *healthy* women
Change in lean mass (Kg / 5 yrs)
Change in fat mass (Kg / 5 yrs)
Change in VAT mass (Kg / 5 yrs)
Increase from initial I_T (Kg/day)
Decrease from initial I_T (Kg/day)
Results in terms of percent change for *healthy* women
% change in lean mass (% / 5 yrs)
% change in fat mass (% / 5 yrs)
% change in VAT mass (% / 5 yrs)
% increase from initial I_T (%/day)
% decrease from initial I_T (%/day)

Figure 5.4: Mass change in *healthy weight* women as a function of changing diet (from baseline). Europeans are represented by red curves, Aboriginal by green, Chinese by blue, and South Asian by purple.

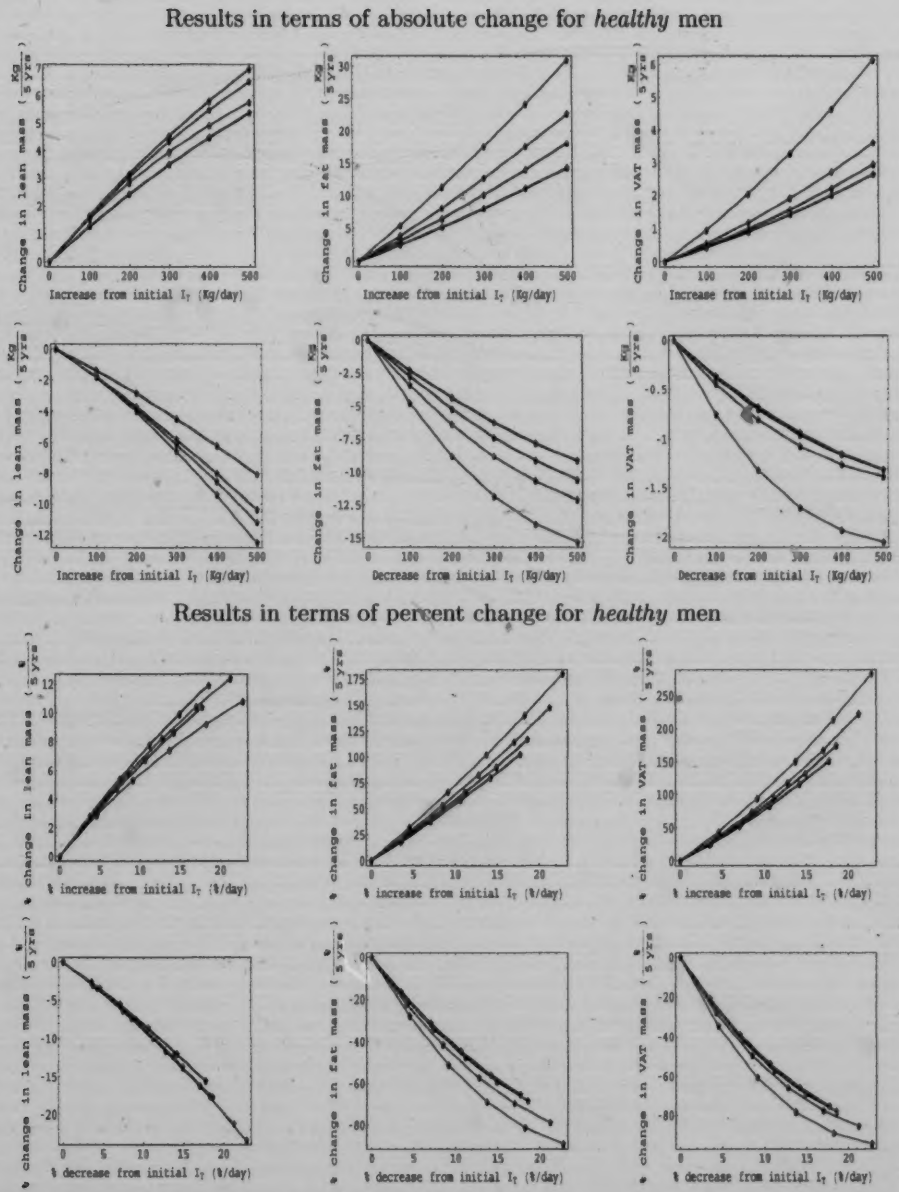

Results in terms of absolute change for *healthy* men
Change in lean mass (Kg / 5 yrs)
Change in fat mass (Kg / 5 yrs)
Change in VAT mass (Kg / 5 yrs)
Increase from initial I_T (Kg/day)
Decrease from initial I_T (Kg/day)
Results in terms of percent change for *healthy* men
% change in lean mass (% / 5 yrs)
% change in fat mass (% / 5 yrs)
% change in VAT mass (% / 5 yrs)
% increase from initial I_T (%/day)
% decrease from initial I_T (%/day)

Figure 5.5: Mass change in *healthy weight* men as a function of changing diet (from baseline). Europeans are represented by red curves, Aboriginal by green, Chinese by blue, and South Asian by purple.

corresponding initial masses.

From Figure 5.5 we see that it is again the case that the Chinese men are least affected by changes in diet. Here, they are gaining (losing) the least amount of all mass types. Also, it is the South Asian men who, like South Asian women, are gaining the most fat and VAT mass. Unlike the previous cases, the European men gain the most amount of lean mass and the South Asian men lose the most amount of lean mass.

Again, in terms of percent changes, we draw similar conclusions. The South Asian men are gaining the greatest percentage of fat and VAT mass and the Chinese men are gaining the least percentage of fat and VAT mass, relative to their initial masses. Also, the European men are gaining the greatest percentage of lean mass and the South Asian men are gaining the least percentage of lean mass, relative to their respective initial lean masses.

5.2.3 Case 3: BMI Range 25 to 29.9 Kg/m^2

The results of this section correspond to overfeeding and underfeeding simulations completed on overweight individuals, as determined by BMI measurements. These individuals have a BMI of 25 to 29.9 Kg/m^2. Figures 5.6 and 5.7 correspond to weight change results for women and men respectively.

In Figure 5.6, the results for women are similar to the previous two cases. Here, it is still true that the Chinese women are the least affected by changes in diet, gaining (and losing) the least amount of lean and fat mass. Here, the Aboriginal women gain (lose) the least amount of VAT mass. However, the Chinese gain (lose) a very similar amount of VAT mass as the Aboriginal. Also, it is again the South Asian women who are the most affected by changes in diet. Here they gain (and lose) the most amount of fat and VAT mass. Unlike the previous cases, the South Asian women also gain (lose) the most amount of lean mass. However, the Aboriginal women gain a very similar amount as the South Asians. Again, similar results are shown in the figures corresponding to percent changes.

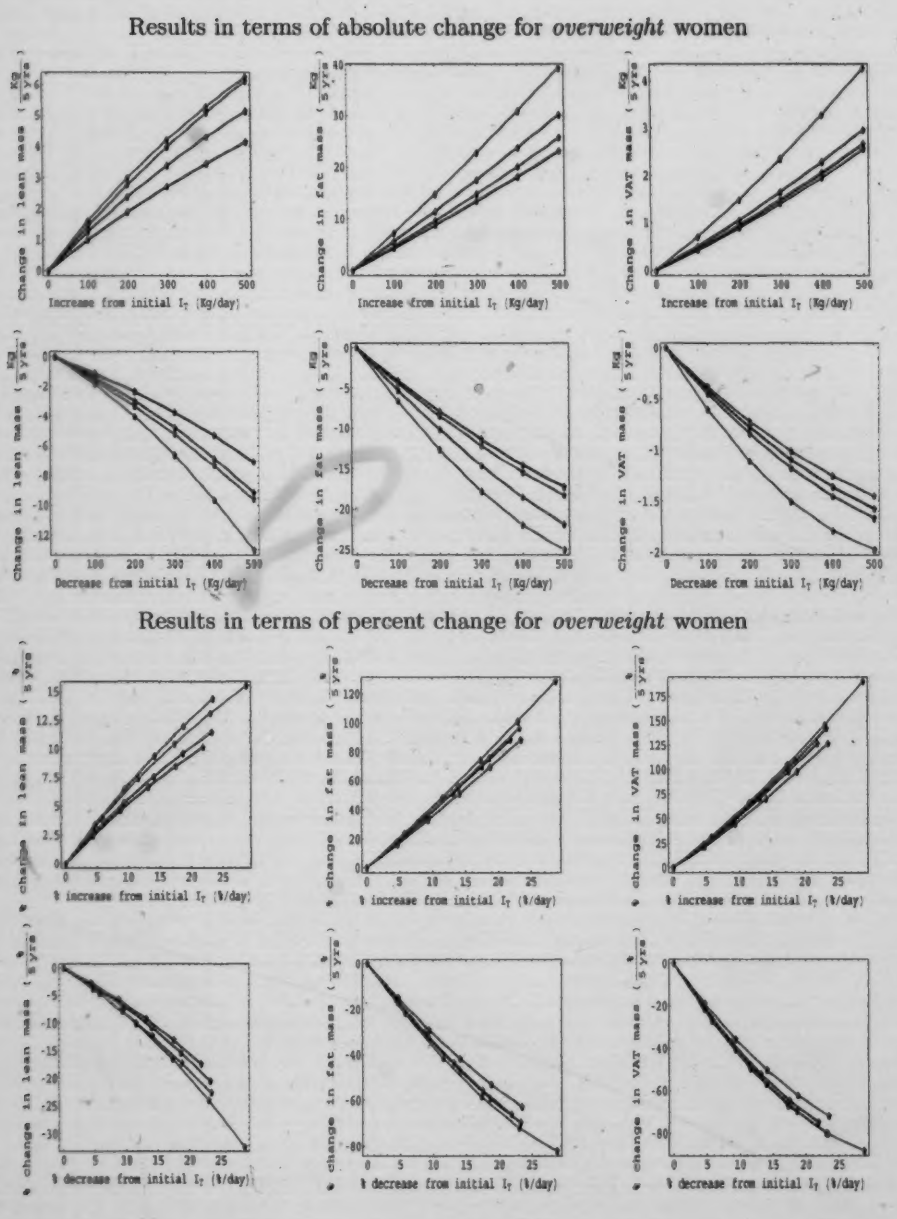

Results in terms of absolute change for *overweight* women
Change in lean mass (Kg / 5 yrs)
Change in fat mass (Kg / 5 yrs)
Change in VAT mass (Kg / 5 yrs)
Increase from initial I_T (Kg/day)
Decrease from initial I_T (Kg/day)
Results in terms of percent change for *overweight* women
% change in lean mass (% / 5 yrs)
% change in fat mass (% / 5 yrs)
% change in VAT mass (% / 5 yrs)
% increase from initial I_T (%/day)
% decrease from initial I_T (%/day)

Figure 5.6: Mass change in *overweight* women as a function of changing diet (from baseline). Europeans are represented by red curves, Aboriginal by green, Chinese by blue, and South Asian by purple.

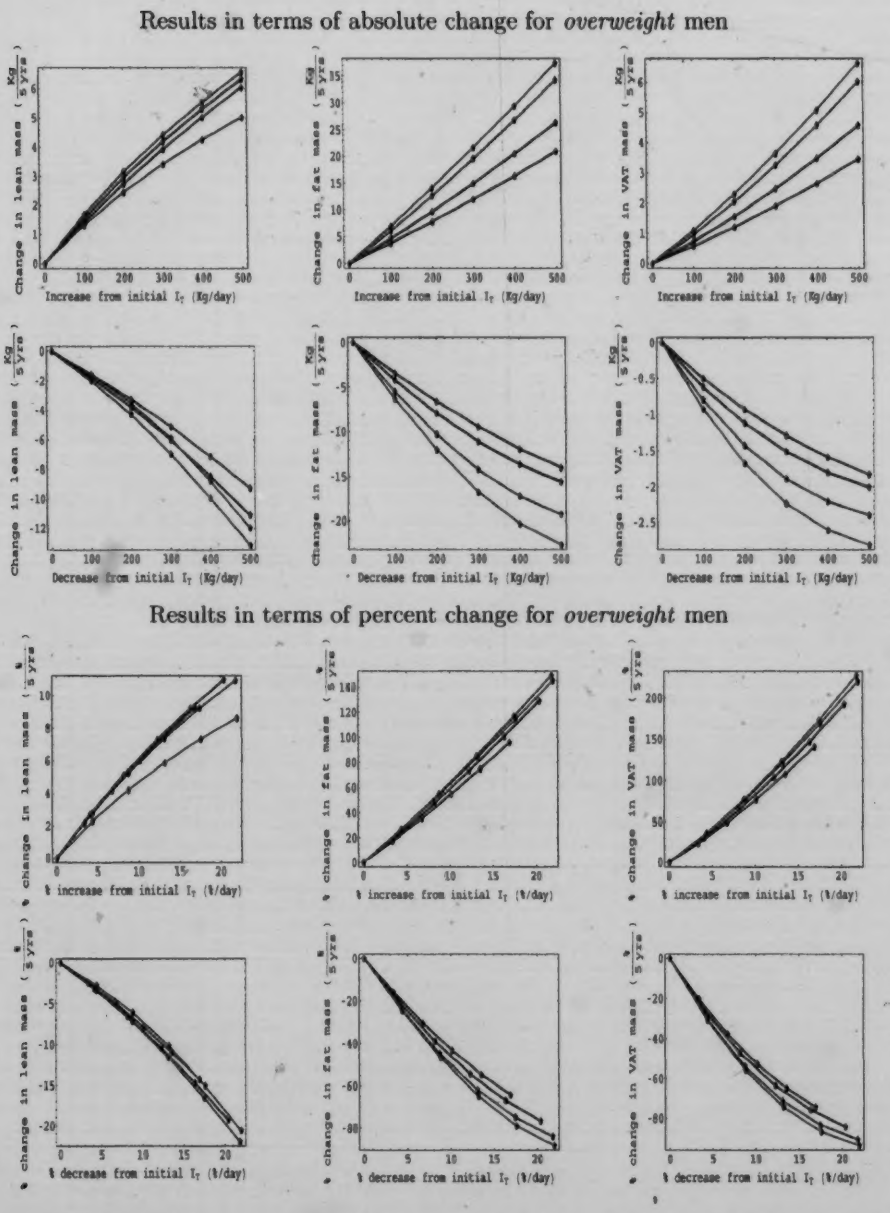

Results in terms of absolute change for *overweight* men
Change in lean mass (Kg / 5 yrs)
Change in fat mass (Kg / 5 yrs)
Change in VAT mass (Kg / 5 yrs)
Increase from initial I_T (Kg/day)
Decrease from initial I_T (Kg/day)
Results in terms of percent change for *overweight* men
% change in lean mass (% / 5 yrs)
% change in fat mass (% / 5 yrs)
% change in VAT mass (% / 5 yrs)
% increase from initial I_T (%/day)
% decrease from initial I_T (%/day)

Figure 5.7: Mass change in *overweight* men as a function of changing diet (from baseline). Europeans are represented by red curves, Aboriginal by green, Chinese by blue, and South Asian by purple.

In Figure 5.7, we see that the results for men are not like those of the previous two cases. Unlike the previous cases, it is the European men who gain (lose) the least amount of fat and VAT mass. Here, the Chinese men gain (lose) the second least amount of fat and VAT mass. Also, it is the South Asian men, who like in the first case, gain the least amount of lean mass. The European men also lose the least amount of lean mass.

The results for weight gain are similar when described in terms of percent changes. Here, the Europeans gain (lose) the least percentage of fat and VAT mass, relative to their initial masses, and the South Asians lose the greatest percentage of fat and VAT mass, relative to their initial masses. The percentages for fat and VAT mass change are slightly greater for Aboriginal men than for South Asian men. This is due to the fact that these men are starting with a lower initial fat and VAT mass than the South Asian men.

5.2.4 Case 4: BMI Range $\geq$ 30 Kg/m^2

The results of this section correspond to overfeeding and underfeeding simulations completed on obese individuals (that is, individuals with a BMI of $\geq$ 30 Kg/m^2). Figure 5.8 and 5.9 correspond to weight gain and weight loss in obese women and men respectively.

From Figure 5.8, we see that women from Chinese and South Asian populations are less affected than individuals in other groups by changes in diet. Like the other three cases, the Chinese women gain (lose) the least amount of lean and fat mass during overfeeding (underfeeding). Also, like the first two cases, the Aboriginal women gain (lose) the most lean mass. Unlike any of the other cases, it is the European women who gain (lose) the most fat mass. Also, unlike the other cases, the South Asian women gain (lose) the least amount of VAT mass.

In terms of percent change, the conclusions are similar. The Aboriginal women are still gaining (losing) the largest percentage of lean mass and the Chinese are still gaining (losing) the smallest percentage of lean mass, relative

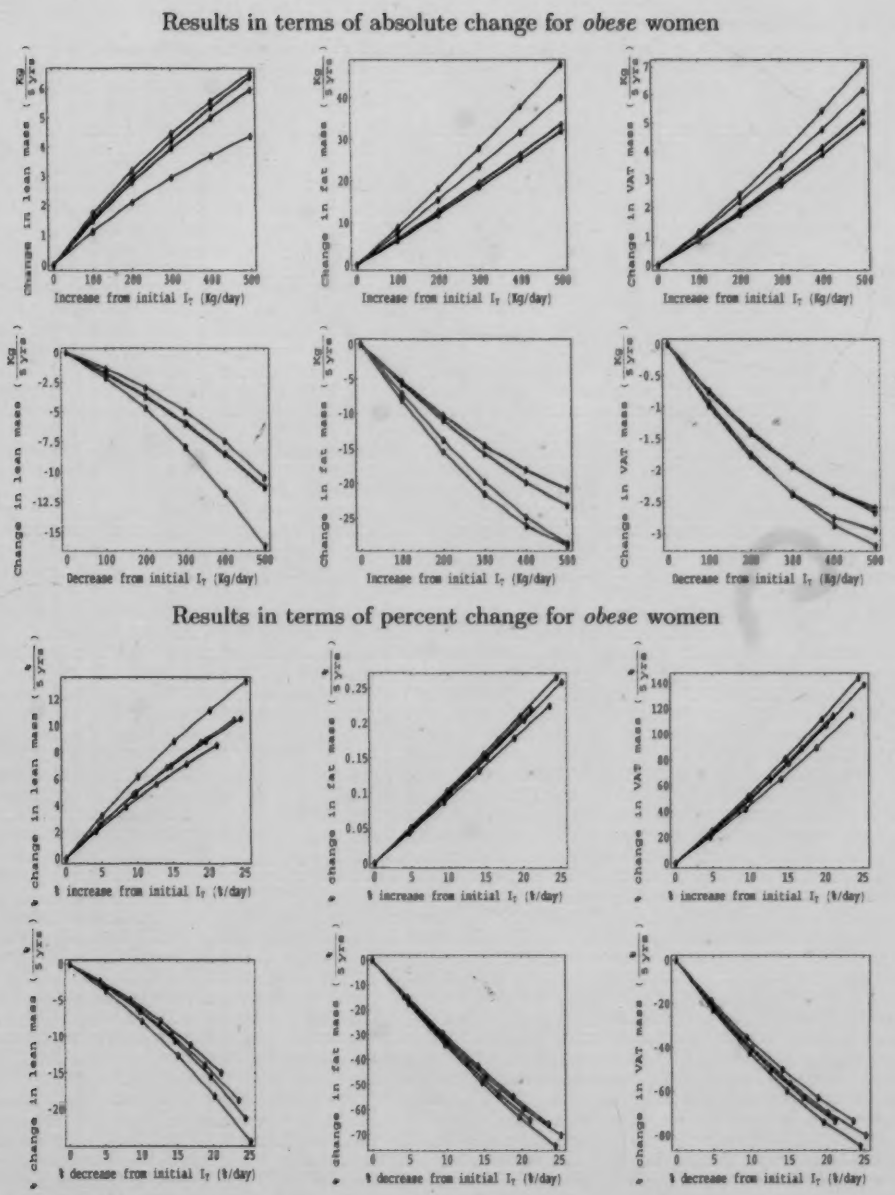

Results in terms of absolute change for *obese* women
Change in lean mass (Kg / 5 yrs)
Change in fat mass (Kg / 5 yrs)
Change in VAT mass (Kg / 5 yrs)
Increase from initial I_T (Kg/day)
Decrease from initial I_T (Kg/day)
Results in terms of percent change for *obese* women
% change in lean mass (% / 5 yrs)
% change in fat mass (% / 5 yrs)
% change in VAT mass (% / 5 yrs)
% increase from initial I_T (%/day)
% decrease from initial I_T (%/day)

Figure 5.8: Mass change in *obese* women as a function of changing diet (from baseline). Europeans are represented by red curves, Aboriginal by green, Chinese by blue, and South Asian by purple.

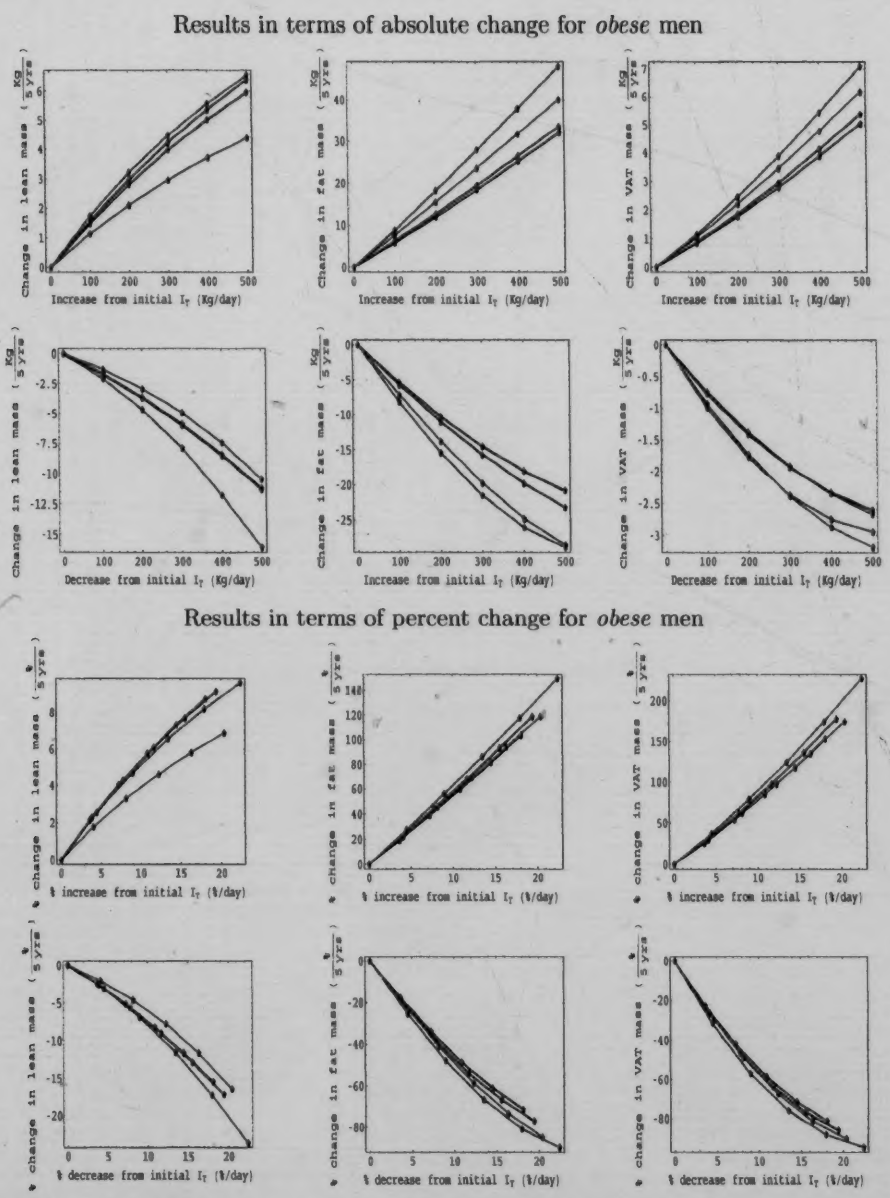

Results in terms of absolute change for *obese* men
Change in lean mass (Kg / 5 yrs)
Change in fat mass (Kg / 5 yrs)
Change in VAT mass (Kg / 5 yrs)
Increase from initial I_T (Kg/day)
Decrease from initial I_T (Kg/day)
Results in terms of percent change for *obese* men
% change in lean mass (% / 5 yrs)
% change in fat mass (% / 5 yrs)
% change in VAT mass (% / 5 yrs)
% increase from initial I_T (%/day)
% decrease from initial I_T (%/day)

Figure 5.9: Mass change in *obese* men as a function of changing diet (from baseline). Europeans are represented by red curves, Aboriginal by green, Chinese by blue, and South Asian by purple.

to their respective initial lean masses. Also, the Europeans are gaining (losing) the largest percentage of fat mass, relative to their initial fat mass, and are gaining (losing) a similar percentage of VAT mass, as compared to the Aboriginals. Here, it is the South Asians, and not the Chinese, who are gaining (losing) the least percentage of fat mass. This is because of differences in their diets. Here, the South Asian's are initially eating less and have a larger initial fat mass. Both of these factors decrease the percentage of fat mass change.

From Figure 5.9, we see that men from Chinese (and European) populations are affected least by changes in diet. Here, they lose (gain) similar amounts of fat and VAT mass. Also, men from south Asian populations are not as affected as other groups by changes in diet, as shown by their changes in lean mass. Like the previous cases, Aboriginal men are the most affected by changes in diet. Here, not only do they lose (gain) the most amount of lean mass, but they also gain (lose) the most amount of fat and gain the most amount of VAT. These results are similar to those corresponding to percent changes, as shown by the bottom two rows of Figure 5.9.

5.3 Discussion of Results

From the previous sections, we have examined how body composition change differs between various ethnic and gender groups. In this section, we aim to explain the results of the previous sections in terms of what is found clinically. We will do this by discussing the results in two separate parts. First, in Section 5.7.1, we will discuss results corresponding to changes in fat and lean mass and second, in Section 5.7.2, we will discuss results corresponding to changes in VAT mass.

5.3.1 Discussion: Changes in Lean and Fat Mass

Obesity has been found to be an independent risk factor for diseases such as atherosclerosis, stroke, and cardiovascular disease (CVD) [22]. By studying

total weight gain and weight loss within the various ethnic groups, we may be able to come to some understanding of why some ethnic groups develop such diseases, while others do not.

In all cases (excluding the last), we have determined that individuals from Chinese populations are the least affected by changes in diet, according to their changes in lean and fat mass. In a recent Canadian study, called 'the Study of Health Assessment and Risk in Ethnic groups' (SHARE) [1], results show that people of Chinese origin have the lowest prevalence of the metabolic syndrome, as compared to individuals from South Asian, Aboriginal, and European populations. In the SHARE study, the metabolic syndrome was defined as an individual having various risk factors such as glucose intolerance, abdominal obesity, elevated triglycerides, low HDL cholesterol levels, as well as cardiovascular disease. The ability for the Chinese to maintain their weight may be an indicator of why they do not develop such diseases.

Also, from our results, we have found that individuals from South Asian and Aboriginal populations are the most affected by changes in diet (based on calculated/simulated changes in lean and fat mass). From the SHARE study, it has been found that individuals from Aboriginal and South Asian populations have an increased susceptibility to develop the metabolic syndrome. Large weight gains may be a reason why these individuals are at such high risk for disease.

It is believed that obesity is the most important factor associated with insulin resistance (a key risk factor for the metabolic syndrome) in South Asian Indians who have settled in other countries, and in India [24]. Also, in an extension of this study, called 'the Study of Health Assessment and Risk Evaluation in Aboriginal People' (SHARE-AP) [2], it is stated that a possible explanation for the high rate of glucose intolerance (also a risk factor for the metabolic syndrome) may be linked to the striking prevalence of obesity and abdominal obesity found in Aboriginal populations. There are many possibilities for why obesity is prevalent among this population. One likely explanation is a change in lifestyle. During the past few decades, these individuals have

gone from a lifestyle that includes a low energy diet and high activity to one that involves a high energy diet and low activity [2].

Also, there are biological explanations for why obesity may be prevalent among the South Asian Indians [24]. One reason is related to a typical obesity phenotype observed in this population. This phenotype consists of a higher percentage of body fat at a lower value of BMI. During periods of weight gain, increased body fat and decreased lean body mass approximately compensate each other, not allowing appreciable increase in the value of BMI. It is speculated that the skeletal structure of South Asian Indians is smaller due to poor nutrition, accounting for less percentage of lean mass (and a greater percentage of fat mass) for a given body weight. These types of skeletal structures have been found in developing countries. Such BMI-defined non-obese individuals may have adverse metabolic effects of excess adiposity.

5.3.2 Discussion: Changes in VAT mass

Here we discuss results of VAT mass gain and loss between the four ethnic/gender groups. These results may be important since recent studies have shown that VAT mass is strongly associated with risk factors for type 2 diabetes. Also, VAT has been shown to be strongly correlated with cardiovascular disease risk factors such as total cholesterol, low HDL cholesterol, triglycerides, apolipoprotein B, blood pressure, insulin resistance and C-reactive protein [22]. The predominant theory is that these associations are mediated by the release of free fatty acids by VAT into the hepatic circulation, thus simulating the release of apolipoprotein B-containing lipoproteins, reducing insulin sensitivity, and increasing plasma glucose values [19].

Our results have shown that, for most ranges of BMI, individuals from South Asian populations accumulate larger amounts of VAT than the other ethnic groups. Other studies show similar results, indicating that intra-abdominal fat accumulates more in South Asian Indians as compared to the other ethnic groups, which may contribute to increased insulin resistance [24].

Previous studies suggest that the high rate of glucose intolerance within Aboriginal populations can be explained not only by the extreme prevalence of obesity within this population, but more specifically by the striking prevalence of abdominal obesity [2]. Our results indicate that individuals from Aboriginal populations do not accumulate as much VAT as the individuals from South Asian populations. However, for some ranges of BMI, they do accumulate more VAT than individuals from the Chinese and European populations. These results may indicate that for some ranges of BMI, overall weight may be more of a risk factor for disease than VAT.

Our results also show that, for most BMI ranges, the Chinese gain (lose) the least amount of VAT mass, as compared to the other ethnic groups. Even though elevated levels of VAT have been observed within Chinese populations (in the past decade), insulin resistance has not been found to be a major issue within this population [1].

Chapter 6

Summary and Conclusions

In this thesis, we have shown that the dynamics of body composition differ between ethnic/gender groups. Specifically, we have determined that different ethnic/gender groups have their own unique value for the Forbes parameter A. This parameter, along with other model inputs such as the intake rate of food I_T, energy expenditure E, and initial body composition (F_i and L_i), affects the outcome of weight gain and weight loss for the various ethnic/gender groups.

Our results have shown that, for all ranges of BMI (excluding the range corresponding to obese individuals), individuals from South Asian populations are more likely to experience large changes in both fat and VAT mass when their diet is perturbed from baseline measurements. It was also shown that individuals from Aboriginal populations are more likely to experience large changes in lean mass when their diet is perturbed from baseline measurements. Since both populations have been prone to develop diseases such as cardiovascular disease and diabetes, these results may help to describe why this is the case. Also, these results suggest that the cause for disease may be different for the Aboriginal and South Asian populations. Specifically, it may be the case that overall obesity is a cause for disease in Aboriginal populations and that large VAT accumulation is a cause for disease in South Asian populations.

Also, for the same ranges of BMI as described above, the Chinese are more likely to experience small changes in all types of masses when their diet is

perturbed from baseline measurements. This may indicate why the Chinese individuals are less likely than the Aboriginal individuals and South Asian individuals to develop diseases that are related to obesity and/or large VAT accumulation.

It is important to note that there is an asymmetry between weight loss and weight gain. From Figures 5.2 to 5.9, it is clear that it is easier to gain fat mass than it is to lose fat mass. The opposite is true for lean mass change. That is, it is easier to lose lean mass than it is to gain lean mass. This trend can be explained by the shape of the Forbes curve (as shown in Figure 2.1). For example, if we start at some arbitrary point along this curve and move to the right (assuming a fixed gain in weight), we will gain a certain amount of fat mass and lean mass. Now, if we move to the left of this same point (assuming the same fixed loss in weight), the absolute value of the decrease in fat mass will be smaller than the absolute value of the increase. Also, the absolute value of the decrease in lean mass will be larger than the absolute value of the increase.

We have also determined that there are limitations to our model. One limitation of our model comes from using Forbes' curve as a description of long-term body composition change. This model only describes approximately 50 % of the variability in our data for each ethnic/gender group (as shown by the R^2 values in Table 4.2). It may be important to consider redefining Forbes' original relationship between F and L, since it is unclear whether the F versus L relationship, described by equation (4.1), is followed over the entire course of weight gain/loss. Specifically, it may be true that another function would better fit the data.

Another limitation of our model is that we have not modeled food intake regulation. Here, we have controlled this input (kept it constant). In general, an individual's eating habits tend to fluctuate, so it may be important to consider a variable intake rate. Also, as stated in Section 4.3, we have defined the energy expenditure E in terms of the total intake rate of food I_T, rather than the separate intake rates I_F and I_L. As suggested in Section 4.3, it may

be important to consider the separate intake rates.

It is also important to note that for the above weight change results, we have used equation (4.3) to describe the substrate utilization $f_F E$, which in turn is used to describe changes in F and L using equations (4.12) and (4.13). It is important to note that here, we have not specified the physiological mechanisms for how substrate utilization adapts to diet I_T, energy expenditure E, and gender/ethnicity (as described by the Forbes parameter A).

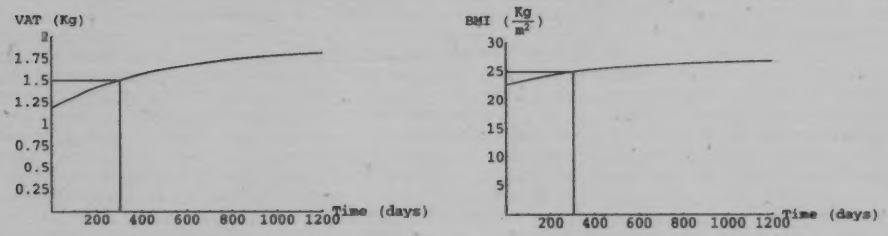
6.1 Future Work

As stated in Chapter 1, anthropometric measurements such as BMI and WHR can be used to identify increased metabolic risk [23]. These methods are more cost efficient than CT scans (used to measure VAT), so are often the preferred method of measurement. However, the definitions of cut offs for such measurements are mostly based on data from Caucasians (mostly Europeans [23]). Studies have shown that, at similar values of BMI, South Asian Indians have significantly greater body fat percentage than do Europeans, in addition to VAT [23, 25]. These results have sparked debate on establishing cut-off parameters based on ethnic background.

Our model can be used to explore this idea further. Specifically, using our model, we can record both VAT mass and BMI over time. If one was able to determine what amount of VAT causes increased risk for disease for various ethnic/gender groups, we would be able to simultaneously track VAT mass and BMI over time and stop our simulation once an unhealthy amount of VAT mass has been reached. At this time, we could record the BMI measurement.

For example, let's assume that for Forbes' original study, (women of height 1.56 to 1.7 m tall) an unhealthy amount of VAT is 1.5 Kg. Recall that, for these women, $A = 10.4$. Now, let's choose a diet consisting of 2200 Kcal/day where 70 % of this diet consists of lean mass and 30 % of this diet consists of fat mass. Let's also choose height $H = 1.63$ meters and an initial body composition such that $F_i = 20$ Kg and $L_i = 40$ Kg. Figure 6.1 shows how

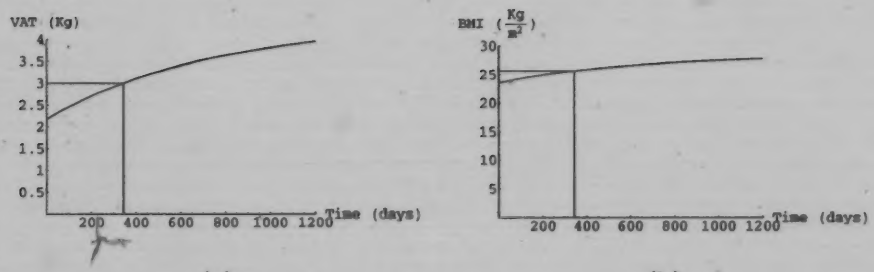
VAT and BMI are simultaneously tracked over time. From this simulation, we find that VAT = 1.5 Kg is reached at time t = 305 days. At this time, the BMI is 24.8 Kg/m^2. This suggests that the BMI cut-off (the cut-off between being healthy and overweight) for European women should be approximately 24.8 Kg/m^2 (the standard cut-off for all men and women is 24.9 Kg/m^2).



(a) (b)

Figure 6.1: (a) VAT mass as a function of time, and (b) BMI as a function of time for Forbes' original group of women.

We can repeat a similar experiment for South Asian men who are at a healthy weight, according to BMI. As shown in Table 5.4, their average baseline diet consists of 2192.87 Kcal/day, where 74.63 % of this diet consists of lean mass and 25.37 % of this diet consists of fat mass. Average height for these men is 1.73 meters and their initial body composition corresponds to F_i = 17.20 Kg and L_i = 53.34 Kg. From Table 4.2, we find that A = 5.59. Now, let's assume that an unhealthy amount of VAT is 3 Kg and let's increase their baseline diet by 200 Kcal/day. From Figure 6.2, it is shown that VAT = 3 Kg is reached at time t = 344 days. At this time, the BMI is 25.6 Kg/m^2, suggesting that the BMI cut-off for South Asian men should be approximately 25.6 Kg/m^2. This value is above the accepted standard value, showing the need for determination of ethnic-specific BMI cut-off parameters.



(a) (b)

Figure 6.2: (a) VAT mass as a function of time, and (b) BMI as a function of time for overfeeding in *healthy weight* South Asian men.

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